CORRELATION OF HISTOMORPHOLOGICAL FEATURES WITH MOLECULAR SUBTYPES OF CARCINOMA BREAST

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I hereby declare that the thesis entitled "**CORRELATION OF HISTOMORPHOLOGICAL FEATURES WITH MOLECULAR SUBTYPES OF CARCINOMA BREAST**" submitted towards partial fulfillment of the requirements for the award of **MD in Pathology** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Aminder Singh**, Associate Professor, Department of Pathology, **Dr. Harpreet Kaur**, Professor & Head, Department of Pathology and **Dr. Kunal Jain**, Associate Professor, Department of Oncology. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

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Dr. Priyanka Seth

LIST OF ABBREVIATIONS

ADH	Atypical Ductal Hyperplasia
ASCO	American Society of Clinical Pathology
BRCA	Breast Cancer gene
CAP	College of American pathologists
CK	Cytokeratin
DCIS	Ductal carcinoma in situ
DNA	Deoxyribonucleic acid
EGFR	Epidermal growth factor receptor
ER	Estrogen receptor
FISH	Fluorescent in situ hybridization
GATA 3	GATA binding protein 3
GDCFP-15	Gross cystic disease fluid protein 15
H&E	Hematoxylin and eosin
HER-2	Human epidermal growth factor receptor-2
IBC	Invasive Breast Carcinoma
IDC	Infiltrating Duct Carcinoma
IHC	Immunohistochemistry
ILC	Invasive Lobular Carcinoma
LCIS	Lobular carcinoma in situ
LVI	Lymphovascular invasion
MBR	Modified Bloom Richardson
NOS	Not Otherwise Specified
NSE	Neuron Specific Enolase

NST	of No Special Type
p63	Transformation related protein 63
PCR	Polymerase Chain Reaction
PR	Progesterone receptor
TDLU	Terminal duct lobular unit
TIL	Tumor infiltrating lymphocyte
TNBC	Triple negative breast cancer
TNM	Tumor, Node, Metastasis

ABSTRACT

Introduction: Breast cancer is the most prevalent type of cancer amongst women and the fifth most common cause of cancer-related mortality worldwide. Histopathological examination has been the gold standard for breast cancer diagnosis. However, a combination of both histopathology and immunohistochemistry is extremely helpful in guiding the lines of treatment and the prognosis.

Aims & Objectives: To correlate histomorphological features with molecular subtypes [Luminal-A, Luminal-B (HER2-negative), Luminal-B (HER2-positive), HER 2/ neu enriched and Triple-negative] of carcinoma breast.

Material & Methods: This was a prospective study conducted in department of Pathology, DMCH, Ludhiana over the period of 1 year from September 15, 2022 to September 14, 2023. All cases of invasive, non-metastatic carcinoma breast undergoing immunohistochemistry testing for molecular subtyping were included in the study.A total of 15,395 specimens were received during this study period, out of which 203 cases were of invasive breast carcinoma on which immunohistochemistry testing was done and were analysed with respect to light microscopic and immunohistochemical findings. Molecular subtypes were determined using expression of ER, PR, HER-2/ neu and Ki-67. Additional IHC markers were put, wherever required. Correlation of molecular subtypes with histomorphological features was done.

Results: Infiltrating Duct Carcinoma, NOS formed the largest histological group with 181 cases (89.2%); out of which 3 cases (1.5%) had medullary pattern. Invasive Lobular Carcinomas comprised 8 cases (3.9%). There were 6 cases of mucinous carcinoma, 3 cases of metaplastic carcinoma and 1 case each of cribriform carcinoma, mixed IBC-NST and invasive lobular carcinoma (85% lobular), encapsulated papillary carcinoma, invasive papillary carcinoma and invasive solid papillary carcinoma. The most commonly found molecular subtype was Luminal-B (54.2% cases), followed by Triple negative (25.1%), HER 2/ neu enriched (13.8%); and Luminal A (6.9%). Statistically significant associations (p-value <0.05) were found between the molecular subtypes and MBR grade, necrosis, skin invasion, microcalcifications and extranodal extension.

Conclusion: Immunohistochemistry is an extremely useful adjunct to histopathology inclassification of breast cancers.

Keywords: Breast, Carcinoma, Histomorphological, Immunohistochemistry (IHC)

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INTRODUCTION

Breast cancer is a disorder marked by uncontrolled cell growth in breast tissue, which can result in the development of a lump in the breast. Each subtype of breast cancer has its unique clinical and pathological characteristics, making it a complex disease.

Breast cancer that develops from the ductal cells is known as ductal carcinoma, while cancer that develops from the lobules is known as lobular carcinoma. Cancer that has migrated to various tissues from its original location is referred to as invasive carcinoma[1].

Both ductal and lobular cancers have the potential to metastasize to different body regions and develop into invasive carcinomas. 80% of all invasive malignancies are invasive ductal carcinomas, while 10% to 15% of cases are invasive lobular carcinomas. Inflammatory breast cancer, Phyllodes breast cancer, and Paget disease of the nipple are additional rare forms of breast cancer[2].

In India, one in nine people are likely to develop cancer in their lifetime. Breast and lung cancers are the leading sites of cancer in females and males, respectively[3]. With 53,592 breast cancer fatalities in 2008, breast cancer is the second most common cause of cancer-related mortality in India, after cervical cancer, with an expected 115,251 new diagnoses[4].

Five-year survival rates calculated in population-based studies on breast cancer in India ranges from 42-48%, while hospital-based studies across India show five-year relative survival rate range from 40-45%. Five-year survival rates of more than 80% also have been reported in many studies from the west[3]. Survival of the breast carcinoma patients is dependent on early detection and timely appropriate treatment[5]. Breast cancer continues to be the most prevalent disease affecting women, with invasive ductal carcinoma accounting for the majority, or more than half, of occurrences, according to the American Cancer Society. Although women are more likely than men to develop breast cancer, men can still develop the disease[2] .

Numerous significant factors are linked to the risk of breast cancer. One of the most important factors is age[6]. Most cases occur in adults who are middle-aged or older. About 77% of all cancers are diagnosed in persons of age 55 years and older[2]. The difference in risk between men and women is a key factor as well. The risk may also be hereditary in nature because it is linked to genetic variables. A small percentage of cases, about 5%, have inherited mutations in the BRCA1, BRCA2, and TP53 genes, which are linked to breast cancer[7]. If a close relative has breast cancer, there is a higher likelihood of the same in the patient as well. Early menarche, reproductive history (nulliparity, late age at first child birth), breastfeeding, late menopausal age, obesity, and ethnicity are reported to be linked with breast cancer in addition to age, gender, and inherited mutations. Breast cancer incidences also appear to be linked to lifestyle choices like physical inactivity, high alcohol consumption and radiation exposure.

As a result, each of the aforementioned factors significantly increase the likelihood that breast cancer will occur in the general population.

There are ways to categorize breast cancer. Stage (TNM staging which applies only to carcinomas and includes both- male and female breasts), grade (based on Nottingham modification of the Bloom Richardson system and involves evaluation of three morphological features including degree of tubule or gland formation, nuclear pleomorphism and mitotic count), histology (WHO 5th edition, 2019 histological classification of invasive breast carcinomas include Invasive breast carcinoma of no special type (NST), microinvasive, invasive lobular, tubular, cribriform, mucinous, invasive micropapillary carcinoma, carcinoma with apocrine differentiation, metaplastic carcinoma, rare and salivary gland-type tumors and neuroendocrine neoplasms), and receptor status are a few of the methods used for classification.

An important strategy for dividing breast cancer into subtypes is receptor status. Cell signalling is controlled by receptors. When hormones or other protein molecules bind to receptors on a cell's surface, the cell undergoes the intended transformation. Receptors

may occasionally be present in breast cancer cells, which really aid in choosing the appropriate course of treatment. It is a standard procedure to examine biopsy samples for receptor presence by immunohistochemistry (IHC). IHC is a method based on the selective binding of specific immunologic reagants to specific antigenic determinants on a cell using a precise lock-and-key mechanism. The site of antibody binding is identified either by direct labelling of antibodies or by secondary labelling.

Estrogen receptor (ER), progesterone receptor (PR), HER2/ neu (HER2), and Ki-67 are the main receptors that are now seen in breast cancer cells. These receptors play a significant role in both the development of cancer cells and the management of cancer[1].

Breast tumors can be divided into three main molecular subgroups based on these receptors: Luminal (ER-positive), HER2 enriched, and Triple negative, each with unique biologic and clinical characteristics. The proliferation of luminal tumors is further separated into two categories, A and B, with group B often having more proliferation than group A does. Luminal A-like cancers are ER/ PR positive, HER2/ neu negative and have low proliferation rate; while Luminal B-like breast cancers are ER positive, PR low positive, have variable HER2/ neu expression (positive or negative) and intermediate or high proliferation rate. Luminal B-like breast cancers tend to have a higher histologic grade than Luminal A-like cancers. The lack of both estrogen and progesterone receptors is a characteristic of the HER2/ neu positive subtype of breast cancer. However, this subtype is distinguished by excessive HER2/ neu protein expression[1]. The Triple negative subtype is an exception. Both progesterone and estrogen receptors are absent from this subtype. Additionally, cells do not overexpress the HER2/ neu protein. Breast cancer is curable. Compared to a few decades ago, the survival rate has grown in the present. This accomplishment can be attributed to both the recent advances in medical research and the growing knowledge regarding breast cancer. Surgery, chemotherapy, or radiation therapy are all options for treating

breast cancer. The combinatorial technique is more advantageous, according to studies[8].

Surgery as a kind of treatment entails essentially removing the breast's cancerous tissue, albeit the entire breast may be saved or the contaminated area may be dissected for this reason. Radiation therapy involves exposing the breast tissue that is afflicted to a little dose of radiation, which kills cancer cells. Depending on the breast cancer subtype, hormone-blocking medications or even monoclonal antibodies may occasionally be given. Drugs that inhibit hormones like progesterone and estrogen aid in the treatment of ER+ and PR+ breast cancer cases. Monoclonal antibodies are made to bind to the HER 2/ neu protein and prevent cancer cells from using it[9]. These subtypes have comparably improved prognoses and survival rates due to the availability of drugs that inhibit estrogen and progesterone as well as monoclonal antibodies for HER2/ neu protein[10].

Chemotherapy is the administration of medications to limit the growth of cancerous cells by obstructing key cancer-progression pathways. TNBC is treated with chemotherapy since it is highly difficult to treat and lacks key receptors. The prognosis and survival rate for TNBC subtype are poor[10].

Hence, the purpose of this study is to compare the histomorphological characteristics of breast cancer with its molecular subtypes because it is known that these molecular subtypes are related to the outcome of therapy. They give potential for improved therapeutic intervention as well as a foundation for comprehending the mechanism of breast carcinogenesis[11]. The meticulous pathological evaluation, in addition to the results of the ER, PR, HER2/ neu, and Ki-67 tests, continues to be of utmost importance in the management of patients with breast cancer[12].

AIMS AND OBJECTIVES

To correlate histomorphological features with molecular subtypes (Luminal-A, Luminal-B, HER 2 / neu enriched and Triple-negative) of carcinoma breast.

REVIEW OF LITERATURE

The milk lines, which run from the axillae to the groin, are two embryological lines along which the breasts (mammary glands), highly modified apocrine sweat glands, develop. On each side of the thorax, only one gland forms in humans, despite the fact that supplementary breast tissue can be found anywhere along the milk lines. Up to adolescence, the growth of the breasts in both sexes is identical. However, following puberty, pituitary, ovarian, and other hormones begin to influence the development of the female breasts.

The hormones of the ovarian cycle regulate the cyclical changes in activity of the breast that occur up until menopause. Like the other female reproductive tissues, the breasts experience progressive shrinkage and evolutionary change after menopause[13].

With 10.4% of all cancer cases among women, breast cancer is the second most common type of non-skin cancer (after lung cancer) and the fifth most common cause of cancer-related mortality globally[14].

RISK FACTORS FOR CARCINOMA BREAST:

Hormonal and genetic factors are the main risk factors for breast cancer development.

Age and estrogen stimulation are the two main risk factors for sporadic malignancies in women. But, a quarter to a third of carcinoma breast cases is familial, resulting from the inheritance of genetic variations that raise the chance of developing carcinoma breast. The DNA repair and genomic stability genes BRCA1, BRCA2 are among the high-risk genes linked to familial breast cancer. In addition to these; TP53, PTEN, STK11, CDH1 and PALPB2 also contribute to high penetrance germline mutations leading to more than four-fold increased risk of breast cancer; while ATM and CHEK2 are moderate penetrance germline mutations which lead to two to four-fold increased risk of development of breast cancer. High penetrance germline mutations contribute to 3%-7%; while moderate penetrance germline mutations lead to 5%-10% of breast cancers[15].

Age: The incidence climbs during the course of a woman's lifespan, reaching its peak between the ages of 75 and 80, after which it begins to slightly decline. The typical age at diagnosis is 51[16] for Indian women, 61 for white women, 56 for Hispanic women, and 46 for African American women. Breast cancer in Indian women is discovered ten years earlier than in Western women, indicating that breast cancer develops in India at a younger premenopausal age[17]. In all age categories, breast cancer is extremely uncommon before the age of 25.

Age of menarche: Those who attain menarche before the age of 11 are 20% more likely to get breast cancer than those who attain menarche after the age of 14. Additionally, a late menopause increases risk.

Age at first live birth: Compared to nulliparous women or women over the age of 35 at their first birth, women who have their first full-term pregnancy at a younger age (20 years) are at half the risk.

First-degree relatives who have breast cancer: The only known risk factor that has been consistently linked to an elevated risk of all subtypes is a family history of breast cancer[18]. The risk of breast cancer rises with the number of first-degree relatives (mother, sister, or daughter) who have the disease, particularly if it struck them while they were young. However, the majority of women lack a family history. The interplay of low-risk susceptibility genes and non-genetic factors is likely what causes the majority of family risk.

Atypical hyperplasia: A history of prior breast biopsies, particularly if they revealed atypical hyperplasia, raises the possibility of developing invasive cancer. Proliferative breast changes without atypia are associated with a lesser increase in risk.

Race/ ethnicity: Although, white women who are not Hispanic get breast cancer at the greatest rate. However, according per Globocan (2012), China, India, and the United States together bear over one-third of the world's breast cancer cases. Between 2008 and 2012, India saw an 11.5% increase in the incidence of breast cancer and a 13.8% increase in its mortality rate from the disease[17].

Estrogen exposure: Oophorectomy reduces endogenous estrogen levels and lowers breast cancer risk by up to 75%. Drugs like tamoxifen and aromatase inhibitors lower the chance of developing ER-positive breast cancer by inhibiting the effects of estrogen or preventing the production of estrogen.

Breast density: Having a high breast radiodensity puts a female at increased risk of getting cancer. High breast densities may be associated with incomplete lobule involution at the conclusion of each menstrual cycle, which could lead to an increase in cells that could convert into cancerous tumors.

Radiation exposure: Radiation exposure, whether from cancer treatments, nuclear accidents, or exposure to atomic bombs raises the risk of breast cancer. High radiation doses and early exposure carry the highest risk. For instance, over the course of 10 to 30 years, women in their teens and early 20s who underwent chest radiation for Hodgkin's lymphoma have a 20% to 30% risk of developing breast cancer.

Carcinoma of the contralateral breast or endometrium: Every year, about 1% of breast cancer survivors experience the development of a second contralateral breast carcinoma. Two well-known anti-oncogenes for breast cancer risk are breast cancer associated genes 1 and 2 (BRCA1 and BRCA2). Chromosomes 13q12 and 17q21 contain BRCA1 and BRCA2, respectively[19]. Women who commonly acquire multiple malignancies and have hereditary mutations in these genes are at a higher risk.

Geographical influence: Breast cancer incidence rates are four to seven times greater in the United States and Europe than they are in other nations. With each generation of immigrants to the United States, the risk of breast cancer rises. Environmental factors, breastfeeding, food, obesity, physical activity, and reproductive history are all likely to have an impact.

Diet: Caffeine consumption may lower the incidence of carcinoma breast, as coffee is attributed to considerably increase plasma enterolactone levels, a phytoestrogen linked to a markedly lower risk of

ER-negative breast cancer[20]. On the other hand, drinking alcohol frequently or heavily raises danger. This connection may be strengthened by decreased folate levels and higher estrogen levels.

Obesity: Obese women under 40 have a lower risk because of the connection to anovulatory periods and lower progesterone levels later in the cycle. For postmenopausal obese women, however, the risk is elevated because of manufacture of estrogens in fat depots. Thus, a high body mass index (BMI) is linked to a worse prognosis for those with a history of breast cancer and an increased risk of post-menopausal breast cancer[21].

Exercise: Exercise helps to boost insulin-like growth factor binding protein-3 (IGFBP-3) and immune system activation and lowers the circulating levels of serum estradiol, androgens, and insulin-like growth factor-1 (IGF1)[22]. Women who do exercise or are physically active likely have a slight protective impact. Premenopausal women, women who are not fat, and women who have had full-term pregnancies see the largest risk reduction.

Breastfeeding: The risk is reduced more significantly the longer a woman breastfeeds. Lactation prevents ovulation and could lead to luminal cell terminal differentiation. The longer and more frequent nursing of newborns is a major factor in the reduced prevalence of carcinoma breast in emerging nations[23].

Environmental toxins: It's possible for environmental pollutants, including organochlorine pesticides, to have estrogenic effects on people. Occupational studies reveal associations between exposure to certain organic solvents and polycyclic aromatic hydrocarbons (PAHs) and breast cancer[24].

IBCs (Invasive Breast Cancers) are heterogeneous diseases with unique molecular, pathologic characteristics, and biological behavior.

A palpable lump usually indicates invasive breast cancer. Over 50% of patients with palpable tumors also have axillary lymph node metastases. Larger carcinomas may attach to the chest wall or result in skin dimpling. Retraction of the nipple may happen when the tumor affects the middle of the breast. Lymphatics may become involved,

obstructing the area's natural skin drainage, leading to lymphedema and skin thickening. In these circumstances, the skin's tethering to the breast by Cooper ligaments is known as a peau d'orange appearance.

Classification of invasive breast carcinomas (WHO 5th Edition, 2019):

Invasive breast carcinoma of no special type (NST)

Microinvasive carcinoma

Invasive lobular carcinoma

Tubular carcinoma

Cribriform carcinoma

Mucinous carcinoma

Invasive micropapillary carcinoma

Carcinoma with apocrine differentiation

Metaplastic carcinoma

Rare and salivary gland-type tumors

- Acinic cell carcinoma
- Adenoid cystic carcinoma
- Secretory carcinoma
- Mucoepidermoid carcinoma
- Polymorphous adenocarcinoma
- Tall cell carcinoma with reversed polarity

Neuroendocrine neoplasms

- Neuroendocrine tumor
- Neuroendocrine carcinoma

Histomorphological features of invasive carcinoma, No Special Type (NST; Invasive Ductal Carcinoma or Invasive Breast Carcinoma NOS or Invasive Ductal Carcinoma or Infiltrating Ductal Carcinoma):

The majority of tumors have an uneven border and are firm to hard upon gross inspection. Because of their small, central pinpoint foci or streaks of chalky-white elastotic stroma and sporadic microscopic foci of calcification, they frequently generate a distinctive grating sound

when cut or scraped. Less frequently, carcinomas are softer in substance and have well-defined borders.

A large and diverse category of lBCs is known as invasive breast carcinoma, NST (IBC, NST), which cannot be morphologically categorized as any of the specific histological categories.

Patterns of tumor in IBC, NST can be any - solid or syncytial infiltrative pattern with arrangement of tumor cells in cords, clusters, and trabeculae. Tumor margins can be highly infiltrative or continuous pushing. Glandular differentiation may be apparent as tubular structures with central lumina in tumor-cell groups. Mitosis/ apoptosis/ necrosis can be seen. Stromal component is extremely variable, ranging from highly cellular fibroblastic proliferation to a scant element of connective tissue. Marked hyalinization may be present. Foci of associated ductal carcinoma in situ are usually present (in as many as 80% cases). Lymphovascular or perineural invasion is seen in 20-30% cases[25].

Microscopic Grading in Breast Carcinoma

(Nottingham Modification of the Bloom-Richardson system):

When properly applied, the Nottingham Modification of the Bloom-Richardson system offers a quick, low-cost, precise, and verified technique for determining a patient's prognosis. The examination of three morphological aspects forms the basis of the this: (a) nuclear pleomorphism, (b) tubule or gland formation, and (c) mitotic count [26].

Tubule formation:

Score 1: Tubule formation constitutes more than 75% of the tumor,

Score 2: Tubule formation constitutes 10-75% of the tumor,

Score 3: Tubule formation constitutes less than 10% of the tumor.

Note: Tubule formation evaluation should take into account the entire tumor.

Nuclear pleomorphism:

Score 1: Nucleus shape and size difference is mild (Mild Nuclear Pleomorphism),

Score 2: Nucleus shape and size difference is moderate (Moderate Nuclear Pleomorphism),

Score 3: Nucleus shape and size difference is significant (Marked Nuclear Pleomorphism).

Mitotic Count:

Mitotic counting process should only be done at the periphery of the tumor and should be started from the most mitotically active areas (the hotspot method). If there is heterogeneity, regions exhibiting a higher frequency of mitoses should be chosen. Once the hotspot is chosen and the first field is considered, subsequent field selection is by random meander through the chosen area, but only fields with a representative tumor cell burden should be assessed. As much as feasible, regions rich in tumors free of normal breast tissue are preferred. The total number of mitoses per 10 high-power fields is recorded. The cut-off points for scoring depend on the field area size, and the microscope used should be calibrated by measuring the diameter of the high-power field (40X objective). Based on these values, mitotic count are scored as 1, 2 and 3.

Score thresholds for mitotic counts based on the diameter of the high-power field and its corresponding area[25]:

Field diameter (mm)	Field area (mm2)	Mitotic count		
		1	2	3
0.40	0.126	≤4	5-9	≥10
0.41	0.132	≤4	5-9	≥10
0.42	0.138	≤5	6-10	≥11
0.43	0.145	≤5	6-10	≥11
0.44	0.152	≤5	6-11	≥12
0.45	0.159	≤5	6-11	≥12

A total score is obtained by adding the scores of tubule formation, nuclear pleomorphism and mitotic count. The histological grade is determined based on the obtained total score [27].

Histologic type scoring:

Total score	Histologic Grade
3-5	1
6-7	2
8-9	3

Special morphological patterns of IBC-NST:

Medullary pattern

Invasive carcinoma with neuroendocrine differentiation

Carcinoma with osteoclast-like stromal giant cells

Pleomorphic pattern

Choriocarcinomatous pattern

Melanotic pattern

Oncocytic pattern

Lipid-rich pattern

Glycogen-rich clear cell pattern

Sebaceous pattern

Medullary pattern: Also called atypical medullary pattern, or cancer with medullary features. It is a medullary or basal-like high-grade breast cancer with characteristics of invasive breast carcinoma NST. These tumors have a high Nottingham grade, pushing margins, syncytial architecture, no glandular structures, necrotic areas, and frequently a noticeable tumor-infiltrating lymphocyte (TIL) infiltrate near the tumor edge. The favorable prognosis of these malignancies appears to be explained by the more recent revelation of the prognostic significance of TILs in high-grade breast cancers [28]. These tumors frequently exhibit geographic necrosis in certain regions. They usually present as triple negative breast cancers, but can variably express basal markers such as CK5/6, CK14, EGFR (HER1), and p53. Weak hormone receptor expression can also occur. Genomic instability is common in these high-grade tumors, and they are highly proliferative.

Invasive carcinoma with neuroendocrine differentiation: It has nests of cells with low- to intermediate-grade nuclei and little cytoplasm. It occurs more commonly in some special types, for example, mucinous carcinomas and solid papillary carcinomas. These cancers are typically hormone receptors (ER and PR) positive and HER 2/ neu negative[29].

Carcinoma with osteoclast-like stromal giant cells: This invasive carcinoma is well-differentiated and has a prominent hypervascular stroma with extravasated erythrocytes and numerous osteoclast-like giant cells. Lymphocytes and monocytes along with mononucleated and binucleated histiocytes, some containing haemosiderin may also be seen. The giant cells show uniform expression of CD68[30] and are negative for S100 and actin. They are also negative for keratin, EMA, ER, and PR. The giant cells are strongly positive for acid phosphatase, NSE, and lysozyme, but negative for alkaline phosphatase, which is indicative of morphological similarity to histiocytic cells and osteoclasts[31].

Pleomorphic pattern: This invasive carcinoma with pleomorphic pattern has wildly pleomorphic, enlarged and bizarre cells, some with multiple nuclei constituting > 50% of the tumor cells in a background of adenocarcinoma or adenocarcinoma with metaplastic spindle and squamous differentiation[32,33]. Although the majority of patients have negative hormone receptor expression, some overexpress HER 2/ neu[32]. Fifty percent of cases are known to have axillary lymph node metastases, most of which include three or more lymph nodes. A lot of patients arrive with advanced illness. A study found that these tumors' existence of a spindle cell metaplastic component is linked to a poor prognosis [34].

Choriocarcinomatous pattern: This pattern mimics the biphasic growth pattern of choriocarcinoma and comprises of multinucleated tumor cells with smudged nuclei extending their irregular, elongated cytoplasmic processes surrounding clusters of monocytic tumor cells. Additionally, abnormal mitotic figures are visible. This pattern may be associated with elevated levels of serum hCG[35].

Melanotic pattern: This pattern shows melanoma and ductal carcinoma combinations. Melan-A focal expression was discovered in 18% of breast tumors in one research[36].

Oncocytic pattern: Due to the abundance of mitochondria, the granular cytoplasm of tumor cells is dense, eosinophilic, and has clearly defined borders[37,38]. In the oncocytic pattern, tumor cells primarily exhibit solid growth with pushing edges that includes sheets, islands, and nests. The nuclei are round, centered, and have prominent nucleoli. ER, PR, and HER 2/ neu expression is variable[25].

Lipid-rich pattern: The tumor cells are large and polygonal, and they have a lot of cytoplasm that is foamy or multivacuolated. The nuclei are atypical, with one or more nucleoli and mild to severe atypia. Mitotic figures are commonly found. Lipid-rich carcinoma is typically categorized as histological grade 3. The majority of cases that are reported are negative for ER and PR[39-41]. High proliferation and HER 2/ neu positive have been observed tendencies. Alpha-lactalbumin, lactoferrin, EMA, and adipophilin are all positively stained by tumor cells; however, CK5/6, CK14, S100, and myoepithelial cell markers are not[25].

Glycogen-rich clear cell pattern: The majority of glycogen-rich clear cell carcinomas (GPCCs) develop as sheets, nests, or cords. It is possible to see papillary, lobular, or tubular patterns, though[42]. The edges and outlines of tumor cells frequently exhibit distinct polygonal shapes. The round or oval nuclei of the tumor cells contain clumped chromatin, and there is an abundance of transparent cytoplasm within them. The clear cytoplasm contains glycogen that is PAS-positive and diastase-sensitive. 35–50% of instances have positive ER, while the majority of cases have negative PR[43]. The published literature varies with regard to HER 2/ neu status.

Sebaceous pattern: Prominent sebaceous differentiation is present. The tumor must originate within the mammary gland parenchyma, lacking any evidence of origin from cutaneous adnexal sebaceous glands. The tumor cells are composed of sebaceous cells having vacuolated, lipid-containing clear cytoplasm. The nuclei of the

sebaceous component vary from small, monomorphic, darkly staining small cells to pleomorphic large cells with prominent nucleoli. The nuclei are mostly eccentrically located. Mitotic figures can be numerous[44]. According to the literature, 3 out of 12 cases, 7 out of 12 cases, and 3 out of 9 cases had positive results for ER, PR, and HER 2/ neu, respectively[45-47].

Microinvasive carcinoma: Breast parenchyma that has been invaded by a carcinoma less than or equal to 1 mm in size. It can be detected anywhere in the breast, usually next to carcinoma in situ (often high grade DCIS). Only when there is obvious evidence of invasion in one focus or multiple clearly distinguishable foci, none of which is larger than 1 mm, microinvasive carcinoma may be identified[25].

Invasive lobular carcinoma (ILC): An invasive breast cancer (IBC) that is composed of dyscohesive cells which are typically scattered or grouped in a single-file linear form is known as invasive lobular carcinoma. It can be multicentric and can affect any portion of the breast. It usually presents as a poorly defined palpable breast mass and also have an increased incidence of contralateral breast involvement (5-19% synchronous). On radiology, a spiculated mass and architectural distortion with infrequent calcification can be seen. Macroscopically, these are irregular and poorly delimited tumors. The etiopathogenesis includes germline mutations affecting CDH1 and E-cadherin loss of function respectively. Histopathologically, the typical pattern is the proliferation of uncoordinated small cells that are either arranged in single-file linear cords that infiltrate the stroma or appear individually scattered across a fibrous connective tissue. Around normal ducts, infiltrating cords usually exhibit a concentric pattern. The nuclei of the neoplastic cells are ovoid, round or notched, and they occasionally feature an intracytoplasmic lumen that frequently has a central mucoid inclusion. Mitoses tend to occur infrequently. Lymphovascular invasion is rare. Low cellularity, slight dyscohesiveness, small nuclear size, undetectable nucleoli, and minor pleomorphism are all cytological characteristics.

Although many ILC patterns have been identified, but none of them exhibit cell-to-cell cohesiveness. Instead, they all resemble the cytological or growth patterns of the classical lLC.

Solid pattern: The characteristic tiny, non-cohesive cells with lobular morphology, which are characteristic of the solid pattern, grow in sheets and undergo more mitoses than the classic type[48].

Alveolar pattern: The cells are primarily organized as globular aggregates of twenty or more cells[49].

Pleomorphic pattern: The growth pattern of lobular carcinoma is retained by pleomorphic lobular carcinoma (PLC), but it also shows higher mitotic count and more pleomorphism than classic lLC (defined as larger cells with marked nuclear pleomorphism, > 4 times the size of lymphocytes / equivalent to that of high-grade ductal carcinoma in situ, with or without apocrine features)[50]. The same pleomorphic cytological characteristics of lobular carcinoma in situ are commonly linked to this pattern. PLC may be made up of signet-ring cells and may show either histiocytoid [51] or apocrine differentiation[52].

Tubulolobular pattern: The combination of a tubular growth pattern and small, homogeneous cells organized in a linear arrangement results in the tubulolobular pattern[53]. Roughly one-third of tubulolobular carcinomas have lobular carcinoma in situ.

Mixed group: This pattern shows an admixture of the classical type with one or more of these patterns[54].

Ductulo-lobular pattern: Both IBC-NST and lobular features of differentiation, when present together, are known as ductulo-lobular carcinomas[55,56].

On immunohistochemistry, Grade 1 or 2 lobular carcinoma usually presents as luminal A subtype whereas grade 3 lobular carcinoma presents as luminal B molecular subtype of carcinoma breast. One of the most consistent molecular alterations in lLC and it's patterns is the loss of expression of the cell-cell adhesion molecule E-cadherin[57-59].

Tubular carcinoma: A low-grade invasive cancer known as tubular carcinoma (TC) is characterized by the presence of round to ovoid or angular tubules with open lumina that make up more than 90% of the

tumor and are lined by a single layer of epithelial cells with low-grade nuclei and sparse mitosis. It usually presents as Luminal A molecular subtype of carcinoma breast[60].

Cribriform carcinoma: An invasive breast carcinoma with >90% of the tumor composed of cribriform islands of epithelial cells with low-grade nuclei and sparse mitosis (grade 1). This is usually ER, PR positive and HER 2/ neu negative tumors[61,62].

Mucinous carcinoma: Pure Mucinous Carcinoma is distinguished by a >90% mucinous component and clusters of low to moderate nuclear grade epithelial tumor cells suspended in extracellular mucin pools.

Hypocellular type A mucinous carcinoma has extensive extracellular mucin pools and sparse tumor cell clusters.

Type B mucinous carcinoma is often hypercellular, with thick tumor cell sheets and comparatively little extracellular mucin [63].

Mucinous carcinoma also presents as Luminal A molecular subtype.

Mucinous cystadenocarcinoma: It is an invasive breast carcinoma with large cystic spaces containing mucin and lined by atypical columnar cells with intracytoplasmic mucin. It is a typical ER and PR negative tumor[64,65].

Invasive micropapillary carcinoma: More than 90% of the tumor is composed of invasive tumor clusters with micropapillary architecture and reversed cell polarity that are positioned in clear spaces. Most of the micropapillary tumors are ER and PR positive, while some of them present as HER 2/ neu positive cancers[66-68].

Carcinoma with apocrine differentiation: More than 90% of tumor cells have an apocrine morphology. Large cells with copious amounts of eosinophilic granular cytoplasm, enlarged nuclei, and prominent nucleoli, mimicking apocrine sweat glands, are the hallmarks of this aggressive cancer. These usually express GCDFP-15[69], are ER, PR negative, and AR-positive; while some cases of this type present as HER 2/ neu positive cancers[70].

Metaplastic carcinoma: Presents as an abnormal spindle cell, mesenchymal, or matrix-producing differentiation in a IBC. It doesn't

contain elements of breast cancer of the traditional kind or ductal carcinoma in situ. It usually presents as triple negative breast cancer[71].

Inflammatory carcinoma: This is staged as T4d and is due to widespread carcinomatous emboli involving the dermal lymphatic vessels. The breast is reddened, warm and associated with widespread edema of the skin. It simulates the appearance of mastitis, however discrete breast mass is not always palpable.

Occult inflammatory carcinoma: Widespread permeation of dermal lymphatics seen in the absence of the clinical features of inflammatory carcinoma[72].

Rare and salivary gland-type tumors:

Acinic cell carcinoma: This is a malignant epithelial neoplasm made up of neoplastic cells that are immunohistochemically positive for EMA and markers of serous acinar differentiation, as well as granular cytoplasm that is both eosinophilic and basophilic and contains intracytoplasmic granules positive for PASD. It is typically immunonegative for ER, PR and HER 2/ neu, while immunopositivity has been reported for AR[73].

Adenoid cystic carcinoma (AdCC): This is an invasive carcinoma with tubular, cribriform, and solid patterns of neoplastic cells made up of both myoepithelial and epithelial cell types; glandular lumina filled with mucins from the epithelium and pseudolumina filled with fibroblasts, basal lamina, and stromal matrix. It is usually characterized as a triple negative tumor of low malignant potential[74,75].

Secretory carcinoma: Exhibits distinct morphological and immunophenotypic characteristics, including extracellular and intracytoplasmic secretions and an immunoprofile that is either weakly ER/PR-positive or triple-negative[76,77].

Mucoepidermoid carcinoma: Defined by the absence of true keratinization and the presence of mucous, basaloid, and epidermoid cells. Majority of the reported cases have been included under triple negative molecular subtype.

Polymorphous adenocarcinoma: Usually has an architectural pattern made up of a large solid area in the center surrounded by thin strands

of monotonous, uniform neoplastic cells. ER, PR, and HER 2/ neu are negative; there is localized and weak immunopositivity for CK7 and E-cadherin.

Tall cell carcinoma with reversed polarity (TCCRP): An invasive breast cancer without myoepithelial cells surrounding the tumor nests, with the neoplastic cell nests primarily structured in a solid papillary pattern made of columnar epithelial cells with nuclei having reversed polarity. For the diagnosis, both the expression of high- and low-molecular-weight cytokeratins and a triple-negative or weakly hormone receptor-positive phenotype are preferred.

Neuroendocrine neoplasms:

Neuroendocrine tumor (NET): Characterized by immunoprofile and histological characteristics typical of neuroendocrine differentiation. NETs are not high-grade neoplasms. For the diagnosis, coexisting ductal carcinoma in situ component is desirable[25].

Neuroendocrine carcinoma (NEC): Characterized by histological characteristics akin to lung small cell and large cell NEC. This tumor is of a high grade. In this case, coexisting ductal carcinoma in situ is also necessary[78,79].

Additionally, there are papillary neoplasms, which are mostly composed of papillae with a fibrovascular core covered by epithelium and, depending upon the type, myoepithelial layer can or cannot be seen. These include Intraductal papilloma, Papilloma with Atypical Ductal Hyperplasia (ADH) or Ductal Carcinoma In Situ (DCIS), Papillary DCIS, Encapsulated papillary carcinoma, Solid papillary carcinoma and Invasive papillary carcinoma.

Staging of Carcinoma Breast:

T– Determined by size of the tumor, skin ulceration, satellite nodules and peau d'orange with dermal lymphatics infiltration

N – Denotes the spread of the tumor to nearby lymph nodes

M –Denotes that cancer has undergone metastasis i.e. it has spread and infiltrated other part(s) of the body.

pTNM Pathological Classification for carcinoma breast:

pT -Primary Tumor

The pathological classification requires the examination of the primary carcinoma with no gross tumor at the margins of resection. When classifying pT, the tumor size is a measurement of the invasive component.

pT: Not assigned (cannot be determined based on available pathological information)

pT0: No evidence of primary tumor

pTis (DCIS): Ductal carcinoma in situ

pTis (Paget): Paget disease of the nipple NOT associated with invasive carcinoma and / or carcinoma in situ (DCIS) in the underlying breast parenchyma.

pT1: Tumor less than or equal to 20 mm in greatest dimension.

pT1mi: Tumor less than or equal to 1 mm in greatest dimension.

pT1a: Tumor greater than 1 mm but less than or equal to 5 mm in greatest dimension.

pT1b: Tumor greater than 5 mm but less than or equal to 10 mm in greatest dimension.

pT1c: Tumor greater than 10 mm but less than or equal to 20 mm in greatest dimension.

pT2: Tumor greater than 20 mm but less than or equal to 50 mm in greatest dimension.

pT3: Tumor greater than 50 mm in greatest dimension.

pT4: Tumor of any size with direct extension to the chest wall and / or to the skin (ulceration or skin nodules).

pT4a: Extension to the chest wall; invasion or adherence to pectoralis muscle in the absence of invasion of chest wall structures does not qualify as T4.

pT4b: Ulceration and / or ipsilateral satellite nodules and / or edema (including peau d'orange) of the skin which do not meet the criteria for inflammatory carcinoma.

pT4c: Both T4a and T4b are present

pT4d: Inflammatory carcinoma (requires the presence of clinical findings of erythema and edema involving at least one-third or more of the skin of the breast).

pN -Regional Lymph Nodes

The pathological classification requires the resection and examination of at least the low axillary lymph nodes (level I). Such a resection ordinarily includes 6 or more lymph nodes.

pNO: If the lymph nodes are negative, but the number ordinarily examined is not met.

pNX: Regional lymph nodes cannot be assessed (e.g., previously removed, or not removed for pathological study).

pN0: No regional lymph node metastasis

pNI: Micrometastases; or metastases in 1 to 3 axillary ipsilateral lymph nodes; and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected.

pNlmi: Micrometastases (larger than 0.2 mm and/or more than 200 cells, but none larger than 2.0 mm).

pNla: Metastasis in 1-3 axillary lymph node(s),including at least one larger than 2 mm in greatest dimension.

pNlb: Internal mammary lymph nodes not clinically detected.

pNlc: Metastasis in 1-3 axillary lymph nodes and internal mammary lymph nodes not clinically detected.

pN2: Metastasis in 4-9 ipsilateral axillary lymph nodes, or in clinically detected ipsilateral internal mammary lymph node(s) in the absence of axillary lymph node metastasis.

pN2a: Metastasis in 4-9 axillary lymph nodes, including at least one that is larger than 2 mm.

pN2b: Metastasis in clinically detected internal mammary lymph node(s), in the absence of axillary lymph node metastasis.

pN3

pN3a: Metastasis in 10 or more ipsilateral axillary lymph nodes (at least one larger than 2 mm) or metastasis in infraclavicular lymph nodes/level Ill lymph nodes.

pN3b: Metastasis in clinically detected internal ipsilateral mammary lymph node(s) in the presence of positive axillary lymph node(s); or metastasis in more than 3 axillary lymph nodes and in Internal mammary lymph nodes with microscopic or macroscopic metastasis detected by sentinel lymph node biopsy but not clinically detected.

pN3c: Metastasis in ipsilateral supraclavicular lymph node(s).

pM- Distant Metastasis

pM1- Distant metastasis microscopically confirmed [80].

Molecular profiling in breast cancer:

Although the primary indicators for adjuvant chemotherapy are clinical staging and routine pathology; but occasionally, this leads to the "overtreatment" of numerous individuals. Despite receiving adjuvant cytotoxic therapy, some patients still acquire metastatic illness. Thus, molecular profiling comes into play.

Breast cancer requires molecular profiling since the disease is heterogeneous and exhibits a range of biological and morphological characteristics. They respond to treatment differently and have diverse clinical behaviors. This classification of cancer aims for a precise diagnosis, predicts disease natural history, behavior, correlates with survival data and response to treatment. It is fundamental to cancer therapeutic decision-making.

Tumors can now be defined by the expression pattern or genomic alterations of many genes simultaneously, due to molecular profiling.

Molecular profiling includes several techniques which offer the possibility of establishing specific genes or gene combinations whose expression level(s) can effectively distinguish different clinical subtypes.

Ancillary Techniques used for classifying breast carcinomas:

Immunohistochemistry/ IHC (protein)

Fluorescent in situ hybridization (FISH)

Gene expression (m RNA)

Comparative genomic hybridization

Gene expression microarray

qRT- PCR

Next generation sequencing (NGS)

Immunohistochemistry (IHC):

IHC of a normal breast reveals that Cytokeratins (8, 18 and 19), Epithelial membrane Antigen (EMA), Mammaglobin, GCDFP-15, and GATA-3 are the most reliable markers for epithelial cells.

High Molecular Weight (HMW) Cytokeratins (CK 14), Smooth Muscle Actin (SMA), Calponin, p63, Smooth Muscle Myosin Heavy Chain, Maspin, and Caldesmon (the latter only in the ductal section) are among the proteins that myoepithelial cells respond to [72].

Response to hormone therapy and chemotherapy is highly correlated with the presence of hormone (estrogen and progesterone) receptors in the tumor tissue.

Breast cancers can be divided into three main molecular subgroups based on their expression of the estrogen receptor (ER), including luminal (ER-positive), HER 2/ neu enriched, and triple negative.

The proliferation of luminal tumors is further separated into two groups, A and B, with group B having more proliferation than group A.

The HER 2/ neu receptor is overexpressed in HER 2/ neu malignancies, typically as a result of HER 2/ neu gene amplification, and these tumors are amenable to treatment with HER 2/ neu inhibitors.

The prognosis is often bad for triple negative breast tumors (TNBCs), which lack ER, PR and HER 2/ neu expression and are frequently accompanied by errors in DNA repair or genomic stability (caused, for example, by the silencing of BRCA1 or TP53 mutation).

Estrogen Receptor(ER)

One DNA-binding domain and two activation function domains make up the nuclear protein ER. IBCs express ER in a range of 65 to 75 percent of cases, and ER plays a significant role in its development. In terms of clinical characteristics, ER-expressing IBCs are frequently more distinct, have a better prognosis, and respond to hormone therapy[81]. One of the most effective prognostic markers in the management of breast cancer is the ER status.

Progesterone Receptor (PR)

Similar to ER, PR is a transcription factor that is expressed in 55% to 65% of IBCs. PR is predominantly regulated by ER and to a lesser extent by growth factors. PR typically co-expresses with ER. Clinically, a loss of PR denotes an increase in aggression and a decrease in hormonal therapy response[81].

ER and PR are codependent variables.

Guidelines for immunohistochemical assessment of ER and PR in breast tissues have been published by the American Society of Clinical Oncology (ASCO) and College of American Pathologists (CAP)[82,83]. The recommendations have made it easier for laboratories to standardize assay performance and reporting.

- The percentage of immunoreactive invasive tumor cells must be reported by the pathologist.
- Because there is evidence that endocrine therapy may be beneficial, tumors with 1% or more invasive cancer cells staining are considered positive (invasive malignancies with 1–10% ER positivity, however, should be described as ER low positive).
- The stain's typical intensity (mild, moderate, or strong) must be mentioned.
- Whether the sample is positive or negative, the pathologist must give an interpretation about the results.
- It is optional to utilize a composite score (Allred, H, or Quick scores) based on percentage + intensity.

Technique:

No later than one hour after being taken from the patient (but ideally much sooner), specimens must be put in 10% neutral buffered formalin. A minimum of 6 hours and no more than 72 hours should pass after fixation. Underfixation of the breast tissue can lead to false-negative ER results and overfixation can lead to false-positive HER 2/ neu results[84]. Sample's normal breast cells are used as internal positive controls, and a comment is provided on the internal control's staining's suitability. When internal controls are present, they should likewise

stain as anticipated. An external control should always be assessed using adequately positive and negative tissues.

ER and PR status of the breast tissues are detected via Allred scoring system. The Allred score is a semi-quantitative technique that involves rating the proportion of positive cells (on a scale of 0-5) and staining intensity (on a scale of 0-3, for negative, weak, moderate and strong, respectively). After that, the proportion and intensity are added together to get final values ranging from 0 to 8. Three to eight is considered positive, whereas zero to two is considered negative[85]. Scores between 3 and 8 indicate a recommendation for hormonal therapy. A score of 1 is not conceivable[86].

ER-positive breast carcinomas typically have superior tumor differentiation. Contrarily, ER-negative breast carcinomas typically have grade 3 histology.

Mucinous, tubular, and lobular carcinomas have a high rate of ER positivity, but most carcinomas with medullary characteristics, metaplastic, and apocrine carcinomas are ER negative.

Molecular profiling initially identified luminal breast cancers as tumors exhibiting gene expression akin to the breast's luminal epithelium. High expression of genes linked to the estrogen receptor (ER), low expression of genes related to the human epidermal growth factor receptor 2 (HER 2/ neu), and low expression of genes related to proliferation are characteristics of luminal A cancers. However, compared to luminal A cancers, luminal B tumors have a poorer prognosis and show low expression of ER-related genes, variable expression of HER 2/ neu related genes, and high expression of proliferation-related genes[87]. Luminal A typically have ER positive, HER 2/ neu negative, Ki-67 low, and PR high; Luminal B (HER 2/ neu negative) molecular subtypes are ER positive, HER 2/ neu negative, and have either Ki-67 high or PR low; Luminal B-like (HER 2/ neu positive) molecular subtypes are ER positive, have HER 2/ neu overexpressed or amplified, with any Ki-67, and any PR[88].

Human epidermal growth factor Receptor– 2 (HER-2)

The transmembrane tyrosine kinase receptor that HER 2/ neu encodes, interacts to extracellular signals and starts a signaling cascade that regulates cell survival and proliferation. In between 12% and 20% of IBCs, the HER 2/ neu gene is amplified or the HER 2/ neu protein is overexpressed, which leads to aggressive tumor growth and a poor clinical outcome[81]. HER 2/ neu, along with EGFR (HER1), ERBB3 (HER3), and ERBB4 (HER4), are growth factor receptors that control healthy cell growth, proliferation, and survival. In healthy breast epithelium, low quantities of HER 2/ neu are found on the cell surface. p185, a transmembrane glycoprotein with tyrosine kinase activity that is a member of the family of epidermal growth factor receptors, is encoded by the oncogene HER 2/ neu (c-erbB-2).

Amplification of the HER 2/ neu gene and overexpression of the protein are present in 15% of invasive breast tumors. Due to an increase in cancer cell motility, proliferation, and angiogenesis, this protein overexpression may then promote a more aggressive cancer biology.

When choosing individuals for HER 2-targeted medicines like trastuzumab, HER 2+ tumor identification is crucial.

It is possible to evaluate HER 2/ neu overexpression and amplification using immunohistochemistry or fluorescent in situ hybridization (FISH), and there is a strong association between these two techniques.

Histology of HER 2/ neu-positive cancers:

High histological grade, extremely pleomorphic nuclei, and more abundant eosinophilic cytoplasm are common characteristics of HER 2/ neu-positive tumors compared to triple-negative tumors. Infiltrative cords or solid cell nests are the common growth patterns, while single file patterns do occasionally appear.

For HER 2/ neu testing in breast cancer, fresh guidelines have been released by the ASCO/CAP; which are as follows[89,90]:

- An immunohistochemical staining of 3+ (uniform, intense membrane staining of more than 10% of invasive tumor cells), a FISH result of more than six HER 2/ neu gene copies, or a FISH ratio (HER 2/ neu gene signals to chromosome 17 signals) of

greater than 2.0 are all considered positive HER 2/ neu results in this joint document.

- Immunohistochemical staining of 0 or 1+, a FISH result of less than 4.0 HER 2/ neu copies per nucleus, or a FISH ratio of less than 2.0 are all indications of a negative HER 2/ neu result.
- Immunohistochemical staining of 2+ (weak and moderate membrane staining in more than 10% of tumor cells), or a FISH ratio of less than are indicators of an ambiguous HER 2/ neu result.
- Reflex testing to FISH is advised in the event of an ambiguous IHC result, and the result obtained is typically accepted as the final result.

When it comes to directing the clinical care of patients with carcinoma breast, HER2/ neu testing is essential. HER2/ neu positive is defined by the College of American Pathologists (CAP) and the American Society of Clinical Oncology (ASCO) as an immunohistochemistry (IHC) score of 3+ (complete and intense membranous staining in more than 10% of the tumor cells) or a score of 2+ (weak to moderate complete membranous staining in more than 10% of the tumor cells or intense membranous staining in less than or equal to 10% of the tumor cells) with gene amplification verified by in situ hybridization (ISH) testing. Cases that don't fit these parameters are regarded as HER2-negative (IHC score 0 and 1+). IHC score 0 is defined as no staining or incomplete and faint/ barely perceptible membranous staining in less than or equal to 10% of the tumor cells, whereas IHC score 1+ stands for incomplete and faint/ barely perceptible membranous staining in more than 10% of the tumor cells[91].

Trastuzumab response is very well predicted by HER 2/ neu positive by either method (IHC or FISH). High grade tumors are frequently HER 2/ neu-positive cancers. Estrogen and progesterone expression are adversely correlated with HER 2/ neu amplification.

Ki-67 (Mib 1 labelling index)

Ki-67 is a nuclear proliferation marker that is expressed in all cell cycle phases, with the exception of G0. In terms of the tumor's clinical behavior, increased Ki-67 expression is typically linked to a higher

grade and more aggressive behavior. Any level of nuclear staining is assessed. There isn't currently a set cutoff point for Ki-67[81]. To help distinguish between the more aggressive Luminal B molecular subtype and the less aggressive Luminal A subtype, a threshold of 14% or 15% has been suggested. Luminal A has a Ki-67 proliferation index of less than 14% or 15%, whereas Luminal B has a Ki-67 proliferation value of higher than or equal to 14% or 15%. Usually, majority cases have a Ki-67 proliferation index value of less than 20%.

Molecular subtypes of carcinoma breast are categorized based on the expression of the four markers described above. The following are the different molecular subtypes[25]:

Luminal A-like

Luminal B-like (HER 2/ neu-negative)

Luminal B-like (HER 2/ neu-positive)

Her-2/neu positive (non-luminal)

Triple-negative type

Luminal A-like is defined as ER and PR-positive, HER 2/ neu-negative Ki-67 low (less than/ equal to 14% or 15%)[92]. Compared to other subtypes, it has the smallest tumor size, the best prognosis, and the lowest recurrence rate[93].

The subclassification of Luminal B-like is luminal B HER 2/ neu-positive and luminal B HER 2/ neu-negative, however either has significant proliferative activity (Ki-67 more than or equal to 14% or 15%) and low PR[92]. Compared to Luminal A, it has an aggressive phenotype and a worse prognosis[93].

Women with early-stage breast cancer (EBC) are likely to develop hormone-receptor positive (HR+) breast cancer (BC), including the Luminal A and Luminal B subtypes[94].

HER-2 overexpression/ gene amplification with absence of ER and PR is referred to be HER 2/ neu positive[92]. High rates of proliferation and a poor prognosis [93] are characteristics of this subtype. HER2/ neu is currently the most significant theranostic test for breast cancer due to its prognostic value.

HER 2/ neu is a target of the monoclonal antibody trastuzumab and other anti-HER 2/ neu drugs. Immunohistochemistry (IHC) assesses the levels of HER 2/ neu protein expression and in situ hybridization (ISH) estimates the status of the HER 2/ neu gene[95].

It is crucial to accurately identify HER-2 status, and the knowledge gained from HER-2 testing can be utilized to analyze biomarkers in the future. To prevent 3+ false positives or 1+ false negatives, scoring standards must be strictly adhered to. Reflux Fluorescence In Situ Hybridization (FISH) testing must be performed in all instances with 2+[96].

The lack of overexpression or amplification of the HER 2/ neu gene, and negative ER and PR expression, is termed as "triple negative." This hormone-lacking breast cancer accounts for 24% of newly diagnosed breast tumors[97] and most breast cancer-related deaths[98]. According to research, this subtype exhibits the most aggressive behavior and produces the worst results[93].

134 cases of male breast cancer were immunohistochemically stained for the following proteins: ER, PR, HER 2/ neu, Ki-67, epidermal growth factor receptor (EGFR), Cytokeratin 5/6 (CK5/6) and CK14 in a study by R. Kornegoor et al. conducted in the Netherlands in 2011. Cases were categorized as triple negative, luminal A, luminal B, HER 2/ neu driven, basal-like, or unclassifiable. Overall, Luminal A (representing 75% of cases) was the most common kind of male breast cancer, followed by Luminal B (21%), and basal-like and unclassifiable triple negative (4%). There were no cases that were HER 2/ neu-driven[99].

Majid et al. projected age-specific and age-standardized women breast cancer incidence for the years 2006 through 2012 using data for the country of Iraq taken from publications of the Iraqi Cancer Registry. IHC results of ER, PR, HER 2/ neu, and Ki-67 tests were examined by frequency of distribution and by age on the breast malignancies of 125 Arabic and 725 Kurdish women. They concluded that particularly among older women, there has been a slight increase in the age-standardised occurrence of carcinoma breast in Iraq[100].

In 521 carcinoma breast patients identified at the University Clinical Hospital of Santiago de Compostela (Spain), Marina Gandara-Cortes et al. in 2012 and 2013 examined the expression of ER, PR, HER 2/ neu, and Ki67. They then classified the cancers using standardised immunohistochemistry, automatic image analysis, and the HER 2/ neu FISH technique. The following percentages of various subtypes were discovered: 6.0% HER 2/ neu-positive, 9.8% luminal B-like (HER 2/ neu-positive), 40.7% luminal A-like, 32.4% luminal B-like (HER 2/ neu-negative), and 11.1% triple negative[101].

From 2009 to 2013, 30 mastectomy specimens were the subject of a 5-year study by Sujoy Kumar De et al. at Davangere, Karnataka, India. These samples were assessed using immunohistochemistry as well as histopathology. The majority of cases were Grade 3 Invasive Ductal Carcinoma, which were identified in patients between the ages of 41 and 60. Of the cases, 56.7% had ER positivity, 50% had PR positivity, and 20% had HER-2/ neu positivity. 10% of HER-2/neu cases had equivocal results. The two most prevalent molecular subtypes identified were Luminal A and Triple Negative[102].

From November 2012 to October 2014, Tiwari et al. in Madhya Pradesh performed a cross-sectional investigation on 70 IBC samples and connected the molecular categorization with their clinicohistopathology. The cases were divided into Luminal A, Luminal B, HER 2/ neu positive, basal-like, and normal-like subtypes using ER, PR, HER 2/ neu, Ki-67, and CK 5/6. Luminal A was identified as the most prevalent molecular subtype (representing 27.1% of all cases), whilst normal-like was identified as the least prevalent molecular subtype (representing 5.7% of all cases). Thus, they came to the conclusion that molecular classification was useful and superior to histological classification, both for clinical care and for short-term prognostic value. Histological classification alone was not able to analyze the biological behavior of the various breast cancers[103].

Inwald et al. assessed the degree to which the common histopathological criteria influence the biology of breast cancer and the impact on treatment and prognosis in their study from 2015. A sum of

4480 female patients with initial, non-metastatic (M0), invasive breast cancer were included in the data from the Clinical Cancer Registry Regensburg in Bavaria, Germany. These patients were diagnosed between 2000 and 2012. ER, PR, HER 2/ neu, and Ki-67 (4-IHC) immuno-histochemical studies identified the tumor biological subtypes as Luminal A (48.4%), Luminal B (24.8%), HER 2/ neu-like (17.8%), and Basal-like (9.0%). Patients with Luminal A tumors had the best 7-year overall survival (OS), whereas those with Basal-like tumors had the worst OS[104].

The Luminal A and B subtypes predict 10-year outcome regardless of the systemic treatment used, as well as residual risk of distant recurrence after 5 years of endocrine therapy, according to a study done by Prat et al. in 2015 on the clinical implications of the intrinsic molecular subtypes of breast cancer. Neoadjuvant trastuzumab or dual HER 2/ neu blocking with trastuzumab/ lapatinib in conjunction with chemotherapy appeared to be most beneficial for patients with HER 2/ neu-enriched illness. The basal-like disease predominated (70–80%) in Triple Negative Breast Cancers (TNBCs). Bevacizumab benefited in the neoadjuvant setting, and docetaxel vs. carboplatin benefited in first-line metastatic disease. The study's findings generally indicated that intrinsic molecular profiling provides clinically relevant information beyond the current pathology-based classifications[105].

Between February 2015 and February 2016, Yu Ji et al. conducted research on 688 breast cancer patients at the Cancer Institute and Hospital of Tianjin Medical University, China. The goal of the study was to examine the relationship between molecular subtype, ER, PR, Ki-67 antigen, p53 gene, and HER-2 expression levels and mammographic density as determined by density analysis software (DAS)/ radiologists visual (RV) categorization. They came to the conclusion that the rates of ER, PR, and HER-2 positivity varied considerably across patients with various RVD grades, and that breast density and molecular pathology in breast cancer were partially linked. After RVD upgrade, HER-2 positive rates exhibited an upward trend[106].

Karangadan et al. conducted a study in 2016 at Lady Hardinge Medical College in New Delhi. Based on the IHC patterns, breast cancer was divided into four molecular subtypes: Luminal A, Luminal B, triple negative, and HER 2/ neu positive. Over the course of three years, 60 breast cancer cases were investigated. The four subtypes were correlated with Ki-67. The triple-negative molecular subtype emerged to be the most prevalent among these 60 cases (40.0%), followed by luminal B (23.3%). The majority of the tumors had modest proliferation indices, although the triple-negative and HER 2/ neupositive subtypes had high proliferation indices. They came to the conclusion that there was a statistically significant (p-value 0.05) association between molecular categorization, histological grade and Ki-67, and that molecular subtypes correlated with the prognosis and aided in the targeted therapy[107].

Between 2012 and 2015, Yunita Setyawati et al. examined the relationship between molecular subtypes and histological grade and lymph node metastases in 247 cases of breast cancer from Dr. Sarjito General Hospital in Yogyakarta, Indonesia. The subtypes with the highest frequency were Luminal A (41.3%), HER2/ neu enriched (19.4%), triple negative (25.5%), and Luminal B (13.8%). 58.7% of the individuals in this 25.5% of TNBC cases had positive CK5/6 staining (basal-like). 41% of the patients had positive lymph nodes[108].

In Bareilly, Uttar Pradesh, India, between July 2014 and June 2017, Mithila Bisht et al. examined the clinicopathological and immunohistochemical profile of 100 IDC breast cases identified in mastectomy specimens. Analysis was done on parameters such as age, location, size of the tumor, metastasis to lymph nodes, histological grading, and hormone receptor status. The bulk of the carcinomas that were diagnosed were of Bloom Richardson Grade II (73%) and 34% of the patients were between the ages of 41 and 50. HER-2/ neu positive and ER/PR negative in 45% of the patients[109].

Swandari Paramita et al. did a retrospective investigation on intrinsic molecular subtypes of carcinoma breast in Indonesian patients in 2019. Patients with invasive ductal carcinoma breast totalled 92 in the

research. To categorize intrinsic molecular subtypes, immunohistochemical labeling with anti-ER, PR, HER-2, and ki-67 antibodies was used. Analysis was done on the relationship between clinical and immunohistochemical variables and intrinsic molecular subtypes of carcinoma breast. The most prevalent intrinsic molecular subtype of carcinoma breast was found to be luminal B (42.39%), followed by HER-2 positive (39.13%), triple-negative (10.87%), and luminal A (7.61%). The study also showed a strong correlation between breast cancer molecular subgroups and patient age. The most prevalent subtype in patients younger than or equal to 35 years old was Luminal B[93].

Soni et al. conducted a cross-sectional study in Rajasthan, India in 2020 on the "histomorphological correlation of breast carcinoma with its molecular classification". There were 500 cases of breast cancer included. They established links between molecular subtypes, histological grade and prognostic variables. Out of these 500 instances, Luminal A (38.2%) was determined to have the highest number of cases, followed by unclassified type (18.2%), basal-like (17.0%), HER-2/ neu enriched (14.8%) and Luminal B (11.8%) (by molecular analysis); and by histological analysis, Infiltrating Duct Carcinoma NOS was followed by lobular carcinomas. A higher grade of IDC, NOS was found in HER-2/ neu enriched and basal molecular subtypes[110].

Ayad Ahmad Mohammed et al. in Iraq performed a retrospective analysis on the clinical characteristics of several molecular subtypes in 311 female patients with breast cancer who had modified radical mastectomy between 2012 and 2020. Invasive Ductal Carcinoma was the most prevalent histological type detected (89.1%), while Luminal B type was the most commonly found molecular subtype (43.7%), with Luminal A coming in second (27.9%). Clinical stages IIB (24.4%) and III A (22.2%) were the most prevalent. Less often occurring tumors were low grade (3.5%) compared to intermediate (51.1%) and high grade (45.3%). The majority of trial participants (85.5%) reported no recurrence of the condition[111].

In a cross-sectional prospective and retrospective investigation from August 2016 to July 2019, Ankit Mittal et al. in Pune categorized 70 cases of breast cancer into various molecular subtypes. The study's molecular classification of breast cancer revealed that the four subtypes were distributed nearly equally, with Luminal A and B each accounting for 22% of cases, and HER 2/ neu enriched and TNBC patients for 25% of cases each. Higher histological grades and pathological stages were observed in HER 2/ neu enriched and TNBC patients, while lower grades and stages were observed in Luminal A and B subtypes. While Luminal B and TNBC molecular subtypes were more frequently linked to lymph node metastases, Luminal B and HER-2/ neu enriched molecular subtypes more frequently revealed DCIS. A noteworthy association was found amongst tumor grade, lymphovascular invasion and the molecular subtypes[112].

A one-year retrospective comparative study involving 148 cases of IBC NST and mixed carcinomas was conducted in Kerala, India, by Neelima Radhakrishnan et al. between January and December of 2019. Included were cases with wide excision, mastectomy with lymph node clearance, sentinel node biopsy, and ER/ PR, HER-2/ neu, and Ki-67 index. Out of the total, Luminal B molecular subtypes accounted for a sizable portion of the cases (60%), with Luminal A following closely at 26%. In 35% of instances, there was lymph node metastases; in 68% of cases, there were lymphovascular emboli with high ki-67 index[113].

MATERIALS AND METHODS

All the trucut biopsies, mastectomy and breast conservation surgery (BCS)/ lumpectomy specimensthose were received in the department of Pathology, Dayanand Medical College and Hospital, Ludhianaand and diagnosed as breast carcinoma cases on histopathology and underwent immunohistochemistry (IHC) testing for molecular subtyping were included in the study.A detailed history including age, sex, parity, family history, menstrual history, lactational history, mammography and metastatic workup (wherever available) was obtained. Slides were subjected to IHC examination under both lower power (100x) and high power (400x) after a detailed Haematoxylin and Eosin (H&E) examination.

Method and collection of data

Inclusion criteria

All cases of carcinoma breast undergoing IHC for molecular subtyping.

Exclusion criteria

All non-neoplastic lesions, non-epithelial tumors of breast and all cases of carcinoma breast in which IHC was not done.

Duration of study

This was a 1 year prospective study from September 15, 2022 to September 14, 2023.

Study Design

This was a prospective study of 1 year duration.

Methodology

In this study, trucut biopsies, mastectomy and breast conservation surgery (BCS)/ lumpectomy specimens received were properly sliced & fixed in 10% formalin for 18-20 hrs. Detailed gross examination was done. The tissue sections were stained with H&E and a detailed

histopathological examination was done as per College of American Pathologists (CAP) Protocol. Sections from tumor were subjected for IHC staining.

For IHC, staining of slides prepared from formalin fixed paraffin embedded tissue (FFPET) on the BenchMark Classic Automated System (from Ventana) was done. Sections from FFPET biopsies were cut using the microtome at 3-4 micron thickness and were mounted onto SuperFrost Plus slides. For each slide, Ventana labels were then printed which included a unique barcode containing all protocol information. The slides were then loaded onto the BenchMark carousel and read by the Ventana Barcode Reader. The automated BenchMark system put the slides through a series of user-defined de-paraffinization and antigen retrieval steps before commencing with the antibody staining. Primary antibody was either applied automatically if in a pre-diluted dispenser or otherwise was manually be titrated onto the slide. The pre-diluted dispensers of the Ultraview Universal DAB detection kit then provided all reagents required for staining. The counterstain and post-counterstain comprise haematoxylin (cat # 760 – 2021) and bluing reagent (cat # 760 –2037). Hence, each case was stained for ER, PR, HER 2/neu, Ki 67 and then subclassified into Luminal-A, Luminal-B, HER 2/ neu enriched and Triple negative subtypes.

HER 2/neu equivocal (2+) cases were subjected to Fluorescence in situ hybridization (FISH) and the final molecular categorization was done accordingly.

Interpretation of IHC study:

- ER/ PR reporting - Nuclear positivity was assessed in tumor cells and percentage of tumor cells showing positivity, staining intensity (graded as 1+ = weak staining, 2+ =moderate staining and 3+ as strong staining were noted).

Allred scoring system was used to combine the intensity and percentage information for an overall score.

Allred scoring system:

Proportional Score (PS) (for ER and PR)	
0	No staining
1	Staining of <1% of tumor cells
2	Staining between 1% and 10% of tumor cells
3	Staining between 11% and 33% of tumor cells
4	Staining between 34% and 66% of tumor cells
5	Staining of ≥67% of tumor cells

Intensity Score (IS) (for ER and PR)	
0	No staining
1	Average weak intensity
2	Average intermediate intensity
3	Average strong intensity

Allred score (range, 0 to 8) = PS+IS·The Allred scoring system [8-point scale (0–8)] was calculated by adding the number representing the proportion of positive cells 0, 1, 2, 3, 4, or 5 to the number reflecting the intensity of the nuclear stain 0, 1, 2, or 3 .

- HER 2/ neu reporting–

Positive (3+): Circumferential membrane staining that is complete, intense and in >10% of tumor cells.

Equivocal (2+): Weak to moderate complete membrane staining and in >10% of tumor cells or complete membrane staining that is intense but within ≤10% of tumor cells.

Negative:

- 1+: Incomplete membrane staining that is faint / barely perceptible and in > 10% of tumor cells
- 0: No staining is observed, or incomplete membrane staining that is faint / barely perceptible and in ≤10% of tumor cells

- Ki-67 labeling index - Percentage of positive nuclei were expressed as a “Ki-67 labeling index” i.e. the percentage of cells expressing Ki-67 determined by counting 1000 cells / slide. A threshold of 14% was taken for helping to discriminate between cases likely to correlate with the more aggressive luminal-B molecular subtype (havingKi-67 proliferation index more than/ equal to 14%) versus the less aggressive luminal-A subtype (havingKi-67 proliferation index < 14%). However, this threshold has not been validated for predicting the response to chemotherapy.

Outcome

Histomorphological and IHC findings of breast carcinomas were documented according to the protocol.

Tools of the data collection:

The primary instrument for gathering data was a self-created, pre-tested structured schedule that was created based on variables to meet the study's goals.

Statistical analysis: The interquartile range (IQR) and median of baseline continuous variables were used, whereas absolute frequencies and percentages were used for categorical variables. Histograms or boxes were used to display continuous data, and bar charts or pie charts were used to display categorical data, depending on the situation. In order to select the most suitable statistical test, we first determined if the data was normally distributed. Kolmogorov-Smirno or Shapiro-Wilk tests were applied in this case.

Univariate analysis was used to obtain a summary of the study individuals' attributes. The Fisher exact test was utilized if any of the anticipated frequencies were less than 5, and the Chi square ($\chi 2$) test was performed to examine the correlation between categorical variables.

Statistical significance was attained when the two-tailed p-value was less than 0.05.

The statistical software for Microsoft Windows called SPSS 26 (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) was used for all statistical computations.

OBSERVATIONS & RESULTS

The present 1 year prospective study (September 15, 2022 to September 14, 2023) was conducted in the Department of Pathology, Dayanand Medical College and Hospital, Ludhiana. All cases of invasive breast carcinoma undergoing immunohistochemistry testing for molecular subtyping were included in the study. All non-neoplastic lesions, non-epithelialtumors of breast and cases of carcinoma breast on which IHC was not done, were excluded.

A total of 15,395 specimens were received during this study period, out of which 203 cases were of invasive breast carcinoma on which immunohistochemistry testing was done and these were clustered into molecular subtypes; LuminalA, Luminal B, HER 2/ neu enriched and Triple negative. Out of these, in our study, Luminal B molecular subtype constituted maximum number of cases (110/ 203; 54.2%).

The age of patient presentation ranged from 28 to 88 years. The youngest patient was 28 years and the oldest was 88 years old. All cases were females, majority of which were post-menopausal (153/203; 75.4%); except for one male patient (aged 50 years). It was observed that maximum breast cancers occurred in individuals with age more than 50 years (131/203; 64.5% cases) with the specific age group of 51-60 years (57/203; 28.1% cases).

Table 1- Age distribution of carcinoma breast (n=203):

Age ranges	Number of cases	Percentage
21-30	1	0.5
31-40	21	10.3
41-50	50	24.6
51-60	57	28.1
61-70	43	21.2
71-80	27	13.3
81-90	4	2.0
Total	203	100.0

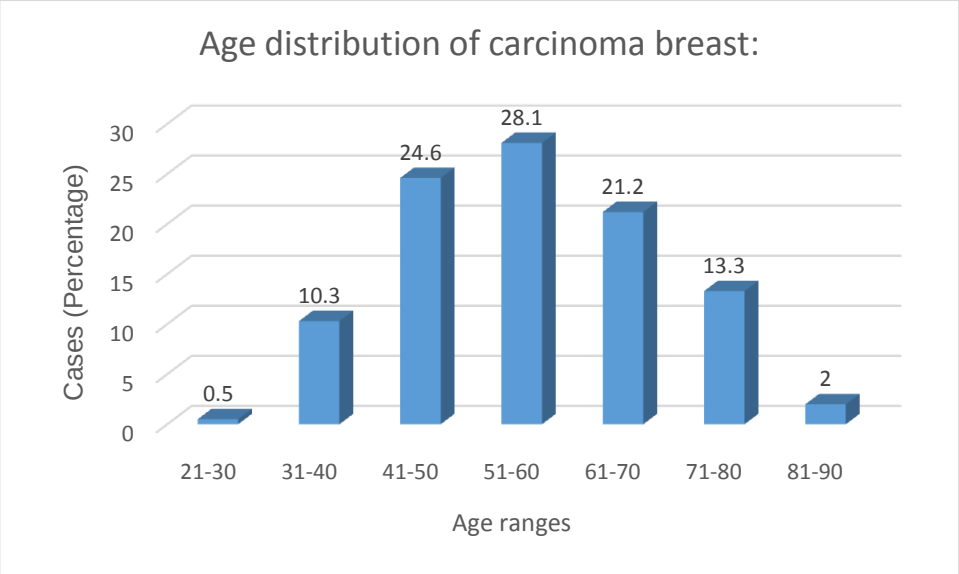

Figure 1: Age distribution of carcinoma breast (n=203)

In the present study, maximum number of specimens received was total mastectomy with axillary dissection (125/203; 61.6% cases). Out of these 125 specimens, there were 5 cases in which trucut biopsies were followed by Modified Radical Mastectomy (MRM) specimens. Second most common type of specimens were of trucut biopsies (49/203; 24.1% cases) followed by total mastectomy without axillary dissection and breast conservation surgery (BCS) specimens(10/203; 4.9% cases each).

Table 2- Distribution of types of breast specimens (n=203):

Types of specimens	Number of cases	Percentage
Total mastectomy with axillary dissection	125	61.6
Trucut biopsies	49	24.1
Total mastectomy without axillary dissection	10	4.9
Breast Conservation Surgery (BCS) specimens	10	4.9
Lumpectomy/ Excision specimens	9	4.4
Total	203	100.0

In the present study, most tumors involved left breast (117/203; 57.6% cases), followed by right (84/203; 41.4% cases). Bilateral breasts were involved in 2 cases (2/203; 1.0% cases). The breast quadrants involved were mentioned in 92 cases and out of these, 51 (55.4%) cases were seen in the upper outer breast quadrant.

Table 3- Distribution of cases according to breast laterality (n=203):

Breast laterality	Number of cases	Percentage
Left	117	57.6
Right	84	41.4
Bilateral	2	1.0
Total	203	100.0

All the tumors were histopathologically classified according to the WHO classification of Invasive Breast Carcinomas (5th edition, 2019). Infiltrating Duct Carcinoma (IDC), NOS formed the largest group with 181 cases (89.2%); out of which 3 cases (1.5%) had medullary pattern. Invasive Lobular Carcinomas comprised 8 cases (3.9%). There were 6 cases of mucinous carcinoma, 3 cases of metaplastic carcinoma and 1 case each of cribriform carcinoma, mixed IDC-NOS and invasive lobular carcinoma (85% lobular), encapsulated papillary carcinoma, invasive papillary carcinoma and solid papillary carcinoma.

Table 4- Distribution of Invasive Breast Carcinomas (n=203):

Histopathological type	Number of cases	Percentage
Infiltrating Duct Carcinoma (IDC), NOS	181	89.2
Invasive Lobular carcinoma	8	3.9
Mucinous carcinoma	6	3.0
Metaplastic carcinoma	3	1.5
Cribriform carcinoma	1	0.5
Mixed IDC-NOS and invasive lobular carcinoma	1	0.5
Encapsulated papillary carcinoma	1	0.5
Invasive papillary carcinoma	1	0.5
Solid papillary carcinoma	1	0.5
Total	203	100.0

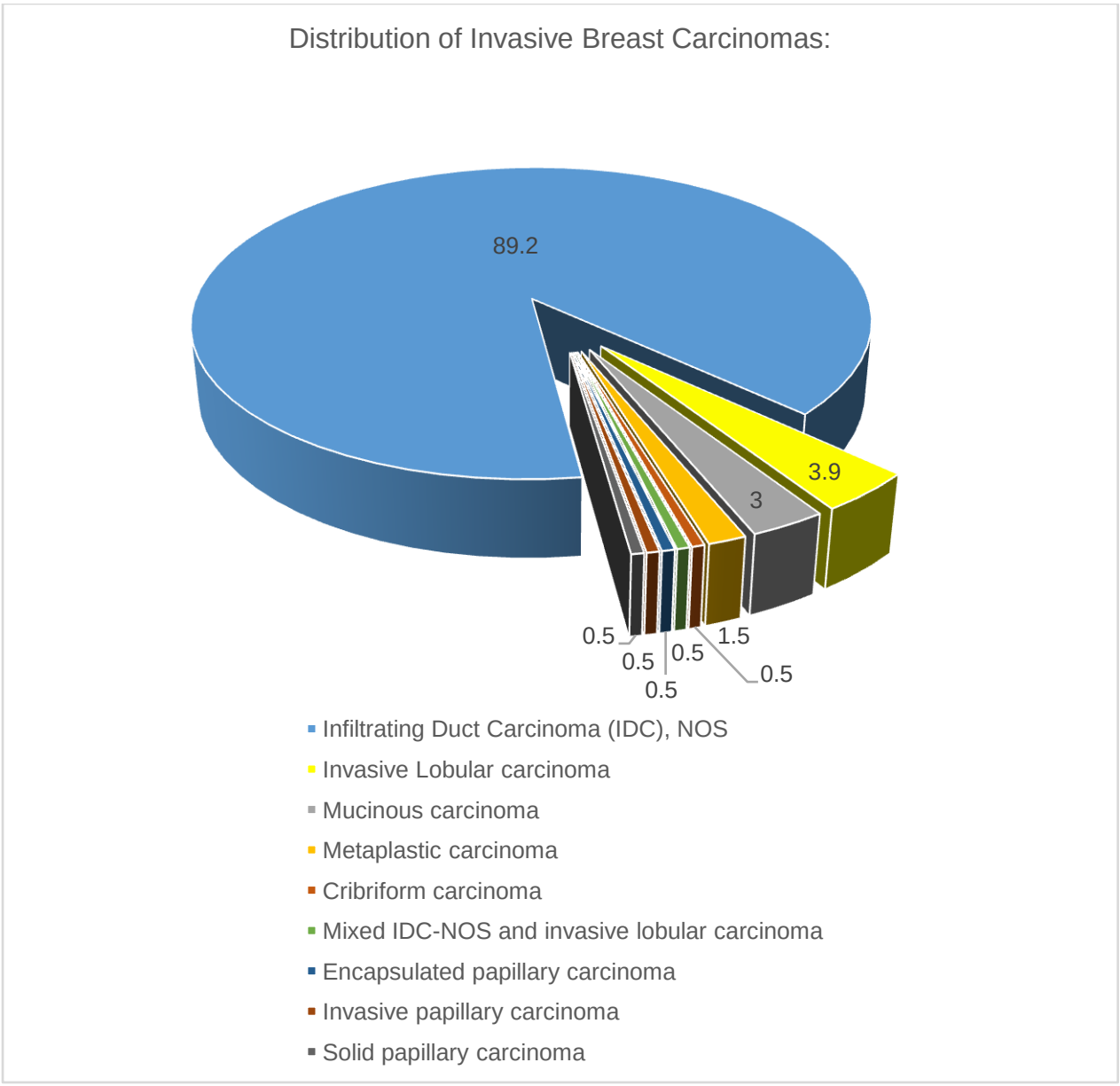

Figure 2- Distribution of Invasive Breast Carcinomas (n=203)

Histologic grading [based on Nottingham Histologic Score or Modified Bloom Richardson (MBR) score] was done for these tumors corresponding to the largest area of invasion. Various other parameters like ‘pT’, Ductal Carcinoma In Situ (DCIS) including its architectural patterns and nuclear grade; Lobular Carcinoma In Situ (LCIS), necrosis, tumor extent including skin, nipple or skeletal muscle involvement, skin invasion, Lymphatic and/ or vascular invasion (LVI), microcalcifications, margins, lymphocytic response at the advancing tumor margins, perineural invasion, lymph node status and extranodal extension were studied. All relevant histological parameters and epidemiological parameters like age were then compared with the molecular subtypes; and statistically significant associations were found between the molecular subtypes and MBR grade, necrosis, skin invasion, microcalcifications and extranodal extension.

Table 5- List of various parameters included in the study:

Table 5 (A)-

Variables		**Number of cases (n, %)**
Laterality	Left	117(57.6)
	Right	84 (41.4)
	Bilateral	2 (1.0)
MBR grade	Grade 1	19 (9.4)
	Grade 2	115 (56.7)
	Grade 3	69 (34.0)
Ductal Carcinoma In situ (DCIS)	Present	51 (25.1)
	Absent	152 (74.9)
Architectural patterns of DCIS	Papillary	3 (1.5)
	Micropapillary	6 (3.0)
	Solid	45 (22.2)
	Comedo	47 (23.2)
	Cribriform	27 (86.7)
	Low	0 (0.0)

Cytonuclear grade of DCIS	Intermediate	28 (13.8)
	High	23 (11.3)
Tumor necrosis	Present	53 (26.1)
	Absent	150 (73.9)
Skin invasion	Ulceration of the overlying skin	4 (2.0)
	Dermis involvement	2 (1.0)
	Epidermis involvement	0 (0.0)
	Absent	197 (97.0)
Lymphatic and/ or vascular invasion	Present	41 (20.2)
	Absent	162 (79.8)
Microcalcifications	Present	38 (18.7)
	Absent	165 (81.3)
Tumor margins	Infiltrating	196 (96.6)
	Pushing	6 (3.0)
	Pushing with focally infiltrating	1 (0.5)
Lymphocytic response at advancing margins	Mild	56 (27.1)
	Moderate	13 (6.4)
	Marked	7 (3.4)
	Not significant	127 (62.6)
Perineural invasion	Present	10 (4.9)
	Absent	193 (95.1)
Lymph node status	Positive	57 (45.6)
	Negative	68 (54.4)
Extranodal extension	Present	39 (68.4)
	Absent	18 (31.6)

Table 5 (B)-

Variables of pTNM staging		Total number of cases (n, %)
'pT' based on tumor size	pT1	23 (14.9)
	pT2	106 (68.8)
	pT3	21 (13.6)
	pT4	4 (2.6)
Lymph nodes status	N0	68 (54.4)
	N1	16 (12.8)
	N2	19 (15.2)
	N3	22 (17.6)

After histopathological examination, breast cancers were clustered into three major molecular groups, luminal (ER-positive), HER 2/ neu enriched and triple negative.

A combination of immunohistochemical markers including ER, PR, HER 2/ neu and Ki-67 were used to categorize these cases into molecular subtypes. Depending on the morphology and results of these markers, additional markers were used in some cases (as and when required). These additional markers were E-cadherin, GATA-3, CK 5/6, SOX 10, CK, p63, Mammaglobin, p40, Vimentin, SMA, EMA, 34βE12, Synaptophysin, Chromogranin A and NSE.

For ER and PR interpretation, ASCO/ CAP guidelines were used and tumors having 1% or more invasive cancer cells staining were regarded as positive. The average intensity of the stain was also included (weak, moderate or strong), and thus, a composite score - Allred score which is a sum of proportion and intensity; and has a range of 0 to 8; was used. Sum of these were obtained on the basis of the following criteria:

Proportional Score (PS) (for ER and PR)	
0	No staining
1	Staining of <1% of tumor cells
2	Staining between 1% and 10% of tumor cells
3	Staining between 11% and 33% of tumor cells
4	Staining between 34% and 66% of tumor cells
5	Staining of ≥67% of tumor cells

Intensity Score (IS) (for ER and PR)	
0	No staining
1	Average weak intensity
2	Average intermediate intensity
3	Average strong intensity

Luminal cancers were further divided into two groups, A and B, that differed mainly in terms of Ki-67 proliferation index, which was low (less than 14%) in group A and high (more than or equal to 14%) in group B. Thus, in the present study, a threshold of 14% was used for classification of Luminal cases into A and B molecular subtypes. However, this threshold does not have any proven validation for the purpose of predicting response to chemotherapy.

In our study, there were 14 Luminal-A cases; all of which had an Allred score of 8/8 for ER, while 10 out of 14 cases had a score of 8/8 for PR. There was 1 case each of 0/8, 3/8, 5/8 and 6/8. In case of immunonegative PR (0/8), Ki-67 proliferation index was estimated to be only 8% in the highest proliferating areas.

Amongst 110 Luminal-B cases, there were 95 cases with an ER interpretation of 8/8, 6 cases with 7/8, 4 cases with 6/8, 3 cases with

4/8 and 2 cases with 3/8; while for PR, 62 cases had an interpretation of 8/8, 9 cases had 7/8, 9 cases had 6/8, 5 cases had 5/8, 7 cases had 4/8, 5 cases had 3/8, 1 case had 2/8 and 12 cases were negative (0/8). HER 2/ neu immunostaining was also interpreted according to ASCO/ CAP guidelines and the following criteria was used.

HER 2/ neu staining pattern	**Score**
0 (Negative)	No staining is observed, or incomplete membrane staining that is faint/ barely perceptible and within ≤10% of tumor cells
1+ (Negative)	Incomplete membrane staining that is faint/barely percep tible and within >10% of tumor cells
2+ (Equivocal)	Weak to moderate complete membrane staining in >10% of tumo r cells or complete membrane staining that is intense but within ≤10% of tumor cells
3+ (Positive)	Circumferential membrane staining that is complete, inte nse, and within >10% of tumor cells

In the present study, 121 cases (59.6%) were interpreted as immunonegative (0 or 1+) for HER 2/ neu; while 45 cases (22.2%) were immunopositive (3+) for HER 2/ neu. There were 37 cases (18.2%) with equivocal (2+) interpretation; out of which 35 underwent FISH testing for final evaluation of the case, out of which 6 cases turned out to be positive.

There were 2 cases with an already positive (3+) HER 2/ neu interpretation; which also underwent FISH testing and turned out to be positive on FISH testing too.

Table 6- FISH analysis of equivocal (2+) HER 2/ neu cases (n=37):

FISH analysis	Number of cases	Percentage
Positive	6	16.2
Negative	29	78.4
Not done	2	5.4
Total	37	100.0

Overall, the most commonly found molecular subtype was Luminal- B with 110 cases (54.2%) followed by Triple negative with 51 cases (25.1%). HER 2/ neu enriched cases constituted 28 cases (13.8 %); while the least cases were found with Luminal A molecular subtype (14; 6.9% cases).

Table 7- Molecular subtypes of invasive breast carcinomas (n=203):

Molecular subtype	Number of cases	Percentage
Luminal-A	14	6.9
Luminal-B	110	54.2
HER 2/ neu enriched	28	13.8
Triple negative	51	25.1
Total	203	100.0

Expression of CK 5/6 was seen in all 51 Triple negative breast cancers (TNBC), 20 out of which showed immunopositivity; thus indicating their basal-like profile. Amongst these, 7 cases showed strong but focal immunostaining, while 13 cases showed strong but diffuse immunostaining.

Similarly, SOX-10 expression was also studied in all TNBC cases and 17 out of the total (51) cases came out to be immunopositive. 2 cases showed weak (<10%) focal immunopositivity, while 2 cases showed moderate focal immunopositivity. 2 cases showed weak but diffuse immunopositivity, 5 cases had moderate diffuse immunopositivity, while

strong diffuse immunopositivity was seen in 6 TNBC cases. None of the cases showed strong but focal immunopositivity.

GATA-3 expression was seen in 38 out of 51 TNBC cases. Only 3 cases showed weak (<10%) focal immunopositivity, rest all showed diffuse immunopositivity. Out of these, 16 cases showed moderate diffuse immunostaining, while 19 cases showed strong diffuse immunostaining with GATA-3.

Combined immunopositivity of both SOX-10 and GATA-3 was seen 12 cases. While, there were 2 cases, in which both SOX-10 and GATA-3 were immunonegative. CK 5/6 showed immunopositivity in those 2 cases.

Amongst 20 CK 5/6 positive cases, there were 8 cases, which were immunopositive for SOX-10 and GATA-3, as well. Hence, in 8 out 51 TNBC cases; CK 5/6, SOX-10 and GATA-3 were positive.

A combination of Synaptophysin, Chromogranin A and NSE showed immunopositivity in a single case of Mucinous carcinoma (showing Luminal-B molecular profile). E-cadherin expression was lost in all 8 cases of Invasive lobular carcinoma. It was also lost in most of the tumor cells in the case of Mixed IDC-NOS and invasive lobular carcinoma (85% lobular), but retained in few tumor cells. In all 3 cases of Metaplastic carcinoma, additional markers including CK, Mammaglobin, p40, Vimentin, SMA and EMA were applied. CK was positive in all 3 cases, Mammaglobin and Vimentin were positive in 2 cases, while p40 was positive was positive in 1 case. None of the cases showed immunopositivity for SMA or EMA. 34βE12 and p63 were used in a single case of IDC with DCIS component.

Table 8- Interpretation of additional markers in TNBCs (n=51):

Additional marker	Pattern of staining	Intensity of staining	Number of cases
CK 5/6	Focal	Weak	0
		Strong	7
	Diffuse	Weak	0
		Strong	13
SOX-10	Focal	Weak	2
		Moderate	2
		Strong	0
	Diffuse	Weak	2
		Moderate	5
		Strong	6
GATA-3	Focal	Weak	3
		Moderate	0
		Strong	0
	Diffuse	Weak	0
		Moderate	16
		Strong	19

The mean age found was 56.3+/-12.4 years; and in this age group also, maximum cases belonged to molecular subtype Luminal-B (31/57; 54.4%).

Table 9- Age distribution of carcinoma breast and the molecular subtypes (n=203):

Age	Luminal-A (n)	Luminal-B (n)	HER 2/ neuenriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
21-30	0	0	1	0	1 (0.5)	23.291	0.180
31-40	0	10	6	5	21 (10.3)		
41-50	2	27	8	13	50 (24.6)		
51-60	3	31	7	16	57 (28.1)		
61-70	6	25	4	8	43 (21.2)		
71-80	2	15	1	9	27 (13.3)		
81-90	1	2	1	0	4 (2.0)		
Total number of cases (n, %)	14 (6.9)	110 (54.2)	28 (13.8)	51(25.1)	203 (100.0)		

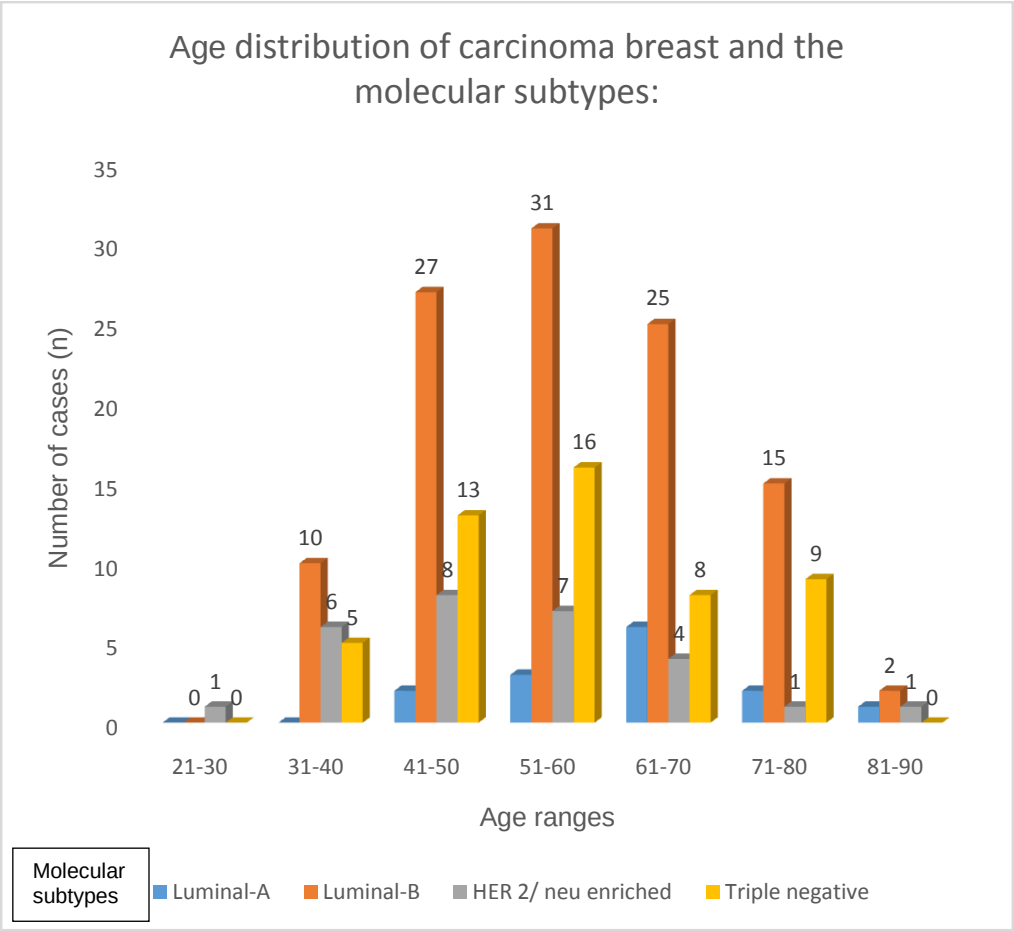

Figure 3- Age distribution of carcinoma breast and the molecular subtypes (n=203)

A statistically strong association was found to be present between histopathological types and molecular subtypes of carcinoma breast with a p-value of <0.05; and out of 181 IDC, NOS cases; 96 cases belonged to Luminal- B molecular subtype.

Table 10- Comparison of histopathological types of carcinoma breast with molecular subtypes (n=203):

Histopathological type	Luminal-A (n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
IDC, NOS	9	96	28	48	178 (89.2)	40.946	0.007
Invasive Lobular carcinoma	3	5	0	0	8 (3.9)		
Mucinous carcinoma	1	5	0	0	6 (3.0)		
Metaplastic carcinoma	0	0	0	3	3 (1.5)		
Cribriform carcinoma	0	1	0	0	1 (0.5)		
Mixed IDC-NOS and invasive lobular carcinoma	0	1	0	0	1 (0.5)		
Encapsulated papillary carcinoma	0	1	0	0	1 (0.5)		
Invasive papillary carcinoma	1	0	0	0	1 (0.5)		
Solid papillary carcinoma	0	1	0	0	1 (0.5)		
Total number of cases (n, %)	14 (6.9)	110(54.2)	28(13.8)	51(25.1)	203(100.0)		

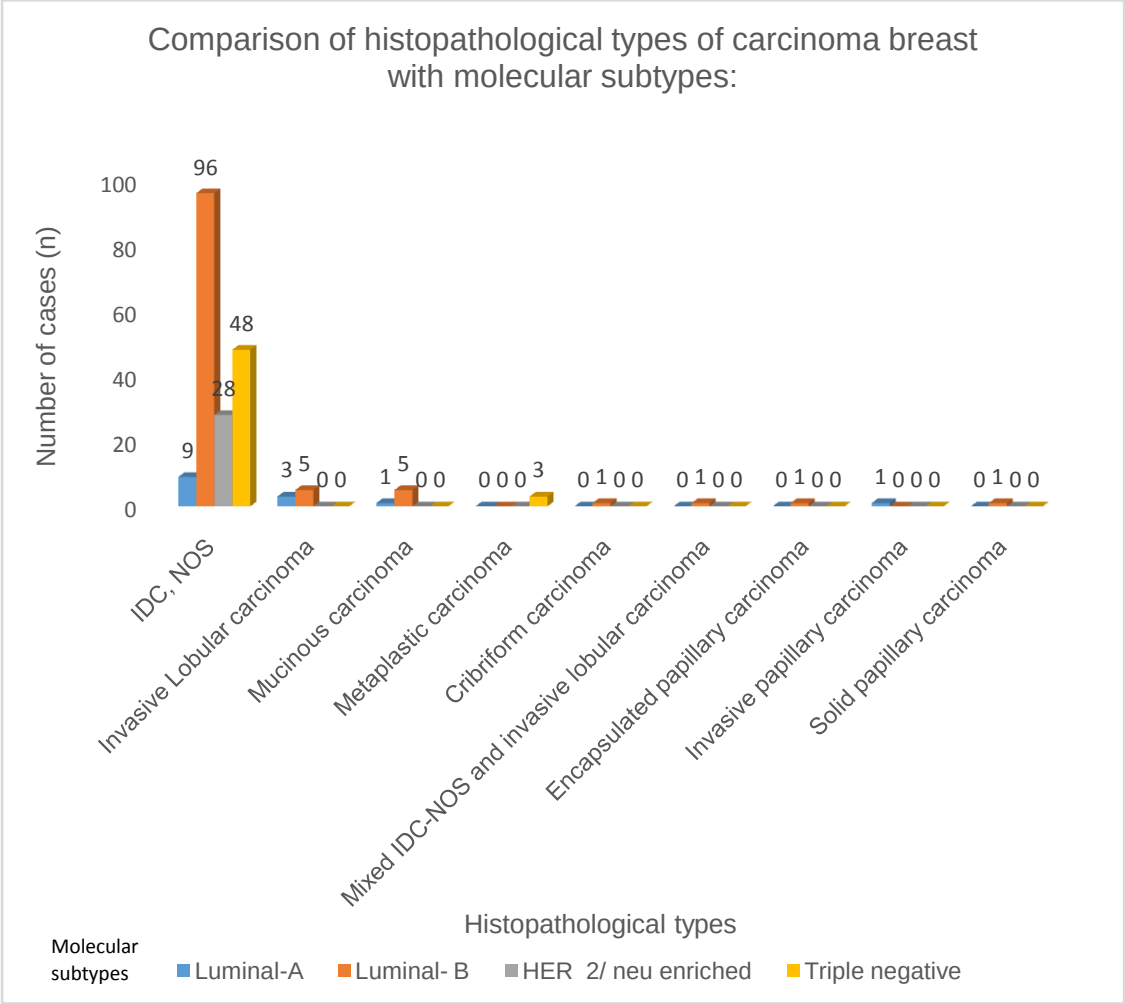

Figure 4- Comparison of histopathological types of carcinoma breast with molecular subtypes (n=203)

In the present study, out of 203 cases of breast cancers,115 (56.7%) were Grade 2 tumors (majority belonging to Luminal-B molecular subtype i.e. 74/115; 64.3% cases with a highly significant p-value of <0.001), 69 were Grade 3 (34.0%) and 19 (9.4%) were Grade 1.

Table 11- MBR grades of carcinoma breast (n=203):

MBR Grade	Number of cases	Percentage
1	19	9.4
2	115	56.7
3	69	34.0
Total	203	100.0

Table 12- Comparison of MBR grade of carcinoma breast with molecular subtypes (n=203):

MBR grade	Luminal-A (n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
1	3	15	1	0	19 (9.4)	49.247	<0.001
2	11	74	14	16	115 (56.7)		
3	0	21	13	35	69 (34.0)		
Total number of cases (n, %)	14 (6.9)	110 (54.2)	28 (13.8)	51 (25.1)	203 (100.0)		

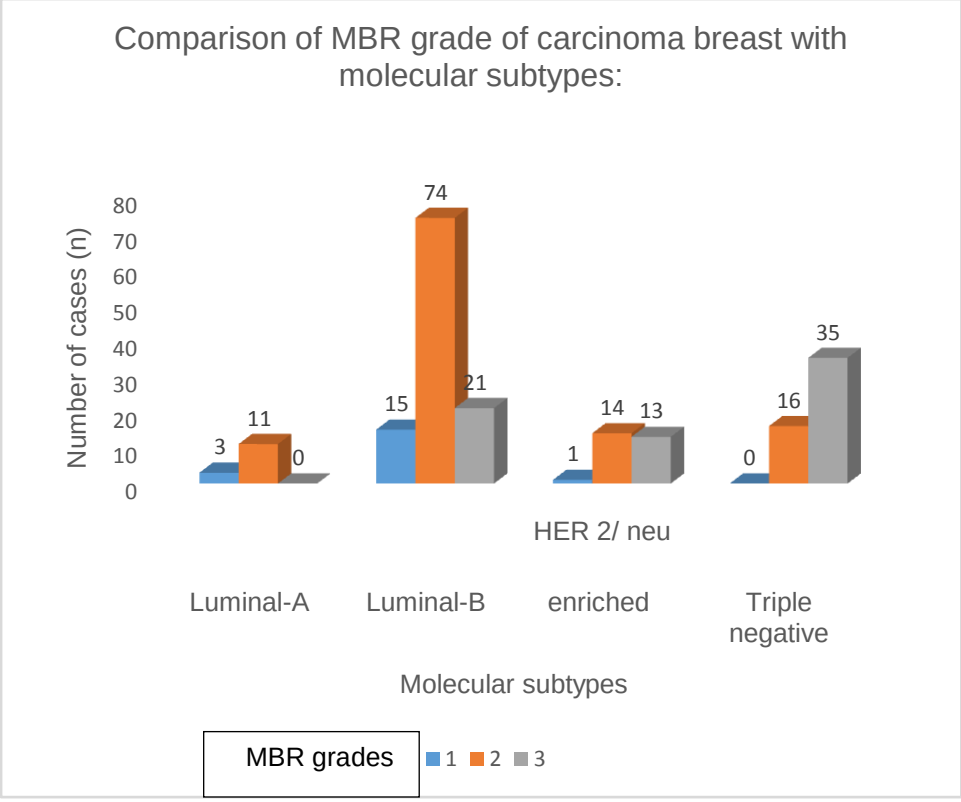

Figure 5- Comparison of MBR grade of carcinoma breast with molecular subtypes (n=203)

In the present study, the tumors (mastectomy/ breast conservation surgery (BCS)/ excision/ lumpectomy specimens; but not trucut biopsies) were classified according to the pTNM classification, maximum cases belonged to T2; i.e. tumor greater than 20 mm but less than or equal to 50 mm in greatest dimension, comprising 106/154 cases (68.8%); followed by T1 i.e. tumor less than or equal to 20 mm in greatest dimension(23/154; 14.9% cases), T3 i.e. tumor greater than 50 mm in greatest dimension (21/154 cases; 13.6%) and T4 i.e. tumor of any size with direct extension to the chest wall and / or to the skin (ulceration or skin nodules)(4/154; 2.6%).

Out of the 106 T2 cases, 59 cases belonged to molecular subtype Luminal B.

Table 13- Distribution of carcinoma breast according to 'pT' (n=154):

'pT' (of pTNM staging) based on tumor size	**Number of cases**	**Percentage**
pT1	23	14.9
pT2	106	68.8
pT3	21	13.6
pT4	4	2.6
Total	154	100.0

Table 14- Comparison of 'pT' of carcinoma breast with molecular subtypes (n=154):

'pT' base on tumor size	Luminal-A (n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
pT1	3	11	1	8	23 (12.9)	8.939	0.370
pT2	7	59	15	25	106 (69.4)		
pT3	0	12	1	8	21 (14.1)		
pT4	0	3	1	0	4 (3.5)		
Total number of cases (n, %)	10 (6.5)	85 (55.2)	18 (11.7)	41 (26.6)	154 (100.0)		

Presence or absence of Ductal Carcinoma in situ (DCIS) component was documented. DCIS component was subclassified on the basis of cytonuclear grade, architectural pattern and percentage of the tumor area.

Small, monomorphic cells that usually grow in a cribriform, micropapillary, or (less frequently) solid pattern involving more than two complete spaces (or measuring more than 2 mm) make up DCIS of low nuclear grade. Microrosettes with tiny luminal spaces can be seen in low-grade solid DCIS. The nuclei are uniform in size and shape, with regular chromatin and inconspicuous nucleoli. In DCIS of low nuclear grade, the nuclei are 1.5–2 times larger than an erythrocyte. Mitosis and necrosis are rare but psammomatous microcalcificationis frequently observed in secretions present in the luminal spaces.

Cells with moderate variability in size, shape, and polarization make up DCIS of intermediate nuclear grade. The nuclei have variably coarse chromatin and sometimes have prominent nucleoli. There may be mitoses and necrosis (either comedo or punctate). Secretions and/or necrotic material may contain microcalcifications.

Atypical, large cells make up DCIS of high nuclear grade; most frequently with a solid architectural pattern. Nonetheless, micropapillary and cribriform patterns could be observed. Typically, spaces in flat DCIS of high nuclear grade are lined by a single layer of large, highly atypical cells (formerly sometimes called the pleomorphic subtype of clinging DCIS). The polarization surrounding luminal spaces is negligible. Large and usually pleomorphic, the nuclei have uneven chromatin, irregular contours, and frequently prominent nucleoli. The nuclei in high-grade DCIS have a diameter of which is more than 2.5 times that of an erythrocyte. Mitoses are usually present. Although it is frequently present, central comedo necrosis bearing microcalcification is not required for the diagnosis.

In the present study, DCIS component was noted in 51 (24.6%) cases; 28 of which had intermediate grade and 23 had high grade DCIS component. Comedo pattern was seen in maximum number of cases

(22.7%) followed by solid pattern (21.7%). Lobular carcinoma in situ (LCIS) was seen in 1 case (0.5%). Maximum breast cancer cases with ductal component belonged to Luminal-B molecular subtype (28 cases) followed by HER 2/ neu enriched type (11 cases).

Table 15- Architectural patterns of Ductal Carcinoma in situ (DCIS) (n=203):

Architectural pattern of DCIS	Number of cases	Percentage
Papillary	3	1.5
Micropapillary	6	3.0
Solid	45	22.2
Comedo	47	23.2
Cribriform	27	86.7

Table 16- Cytonuclear grades of Ductal Carcinoma in situ (DCIS) (n=203):

Grade of DCIS	Number of cases	Percentage
Low	0	0.0
Intermediate	28	13.8
High	23	11.3
No DCIS	152	74.9
Total	203	100.0

Table 17- Distribution of cytonuclear grades of Ductal Carcinoma in situ (DCIS) in carcinoma breast and molecular subtypes (n=203):

DCIS grade	Luminal-A (n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
Low	0	0	0	0	0 (0.0)	7.702	0.630
Intermediate	1	17	6	4	28 (13.8)		
High	1	11	5	6	23 (11.3)		
No DCIS	12	82	17	41	152 (74.9)		
Total number of cases (n, %)	14 (6.9)	110 (54.2)	28 (13.8)	51 (25.1)	203 (100.0)		

In the present study, necrosis was seen in 53/203 (26.1%) cases; out of which 25 cases were Luminal-B type followed by 17 cases belonging to Triple negative molecular subtype. A statistically significant association was found to be present between the status of necrosis and the molecular subtypes of carcinoma breast with a p-value of <0.05.

Table 18- Status of necrosis (n=203):

Tumor necrosis	Number of cases	Percentage
Present	53	26.1
Absent	150	73.9
Total	203	100.0

Table 19- Correlation of necrosis with molecular subtypes (n=203):

Tumor necrosis	Luminal-A(n)	Luminal-B (n)	HER 2/ neu Enriched(n)	Triple negative(n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
Present	0	25	11	17	53 (26.1)	9.821	0.020
Absent	14	85	17	34	150 (73.9)		
Total number of cases (n, %)	14 (6.9)	110 (54.2)	28 (13.8)	51 (25.1)	203 (100.0)		

According to College of American Pathologists (CAP) protocol, there are multiple ways that a carcinoma breast can involve the skin, i.e. DCIS involving nipple epidermis (Paget disease of the nipple), carcinoma directly invading into the dermis or epidermis without skin ulceration (does not change the T classification), or carcinoma directly invading the dermis or epidermis with skin ulceration (classified as T4b), ipsilateral satellite skin nodules, and dermal lymphovascular invasion. Carcinoma present within lymphatic spaces in the dermis is often correlated with the clinical features of inflammatory carcinoma (diffuse erythema and edema involving one-third or more of the breast), and such cases would be classified as T4d. In the absence of the clinical features of inflammatory carcinoma, this finding remains a poor prognostic factor but is insufficient to classify a cancer as T4d.

In the present study, status of skin invasion was noted [wherever applicable; i.e. in mastectomy and breast conservation surgery (BCS) specimens] and was seen only in 6 cases, constituting 4.2% of the total cases. There were 4 cases with ulceration of the overlying skin and 2 cases with dermal involvement. Epidermis was free of tumor in all cases included in the study.

A highly statistically significant correlation was seen between the status of skin invasion and the molecular subtypes of carcinoma breast with p-value of <0.001.

Table 20- Status of skin invasion in carcinoma breast (n=145):

Skin invasion	Number of cases	Percentage
Ulceration of the overlying skin	4	2.8
Involvement of the dermis	2	1.4
Involvement of the epidermis	0	0.0
Absent	139	95.8
Total	145	100.0

Table 21- Correlation of skin invasion in carcinoma breast with molecular subtypes (n=145):

Skin invasion	Luminal-A (n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative(n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
Ulceration of the overlying skin	0	3	1	0	4 (2.8)	229.588	<0.001
Involvement of the dermis	0	1	1	0	2 (1.4)		
Involvement of the epidermis	0	0	0	0	0 (0.0)		
Absent	9	79	15	36	139 (95.8)		
Total number of cases (n, %)	9 (6.2)	83 (57.2)	17 (11.7)	36 (24.8)	145 (100.0)		

Lymphatic and/ or vascular invasion (LVI) was documented according to the College of American Pathologists (CAP) protocol which is as follows:

1. LVI must be diagnosed outside the border of the invasive carcinoma. The most common area to find LVI is within 1 mm of the edge of the carcinoma.
2. The tumor emboli usually do not conform exactly to the contours of the space in which they are found. In contrast, invasive carcinoma with retraction artifact mimicking LVI will have exactly the same shape.
3. Endothelial cell nuclei should be seen in the cells lining the space.
4. Lymphatics are often found adjacent to blood vessels and often partially encircle a blood vessel.

LVI was seen in 41/203 (20.2%) cases; out of which 21 cases belonged to molecular subtype Luminal-B.

Table 22- Status of Lymphatic and/ or vascular invasion (n=203):

Lymphatic and/ or vascular invasion	Number of cases	Percentage
Present	41	20.2
Absent	162	79.8
Total	203	100.0

Table 23- Correlation of Lymphatic and/ or vascular invasion with molecular subtypes (n=203):

Lymphatic and/ or vascular invasion	Luminal-A(n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
Present	1	21	9	10	41 (20.2)	4.073	0.254
Absent	13	89	19	41	162 (79.8)		
Total number of cases (n, %)	14 (6.9)	110 (54.2)	28 (13.8)	51 (25.1)	203 (100.0)		

Microcalcifications were noted in 38 (18.7%) of our study cases and formed a significant association when compared with the molecular subtypes ($p<0.05$). Maximum cases (26 in number) belonged to Luminal-B molecular subtype.

Table 24- Status of microcalcifications (n=203):

Microcalcifications	Number of cases	Percentage
Present	38	18.7
Absent	165	81.3
Total	203	100.0

Table 25- Comparison of status of microcalcifications and molecular subtypes (n=203):

Microcalcifications	Luminal-A (n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
Present	5	26	4	3	38 (18.7)	10.291	0.0168
Absent	9	84	24	48	165 (81.3)		
Total number of cases (n, %)	14 (6.9)	110 (54.2)	28 (13.8)	51 (25.1)	203 (100.0)		

In the present study, maximum cases had infiltrating tumor margins (196/203; 96.6% cases); majority of which Luminal-B type (107 cases). While pushing margins were seen in only 6 (3.0%) cases. There was 1 case (0.5%) with pushing and focally infiltrating margins.

Table 26- Status of tumor margins (n=203):

Tumor margins	Number of cases	Percentage
Infiltrating	196	96.6
Pushing	6	3.0
Pushing with focally infiltrating	1	0.5
Total	203	100.0

Table 27- Correlation of tumor margins and molecular subtypes (n=203):

Tumor margins	Luminal-A (n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
Infiltrating	13	106	28	49	196 (96.6)	4.928	0.927
Pushing	1	3	0	2	6 (3.0)		
Pushing with focally infiltrating	0	1	0	0	1 (0.5)		
Total number of cases (n, %)	14 (6.9)	110 (54.2)	28 (13.8)	51 (25.1)	203 (100.0)		

Significant lymphocytic response (mild, moderate and marked) at the advancing tumor margins was noted in 76/203 (37.4%) cases; majority of which belonged to molecular subtype Luminal-B (40 cases).

Table 28- Status of lymphocytic response at the advancing tumor margins (n=203):

Lymphocytic response at the advancing margins	Number of cases	Percentage
Mild	56	27.6
Moderate	13	6.4
Marked	7	3.4
No significant response	127	62.6
Total	203	100.0

Table 29- Correlation of lymphocytic response at the advancing tumor margins and molecular subtypes (n=203):

Lymphocytic response at the tumor margins	Luminal-A (n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
Mild	2	33	7	14	56 (27.1)	9.467	0.693
Moderate	1	4	3	5	13 (6.4)		
Marked	0	3	1	3	7 (3.4)		
No significant response	11	70	17	29	127 (62.6)		
Total number of cases (n, %)	14 (6.9)	110 (54.2)	28 (13.8)	51 (25.1)	203 (100.0)		

In the present study, perineural invasion was noted in only 10 (4.9%) cases; 8 of which belonged to Luminal-B type on immunohistochemistry; followed by 1 case each of HER 2 /neu enriched and Triple negative molecular subtypes.

Table 30- Status of perineural invasion (n=203):

Perineural invasion	Number of cases	Percentage
Present	10	4.9
Absent	193	95.1
Total	203	100.0

Table 31- Correlation of perineural invasion and molecular subtypes (n=203):

Perineural invasion	Luminal-A (n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
Present	0	8	1	1	10 (4.9)	2.982	0.394
Absent	14	102	27	50	193 (95.1)		
Total number of cases (n, %)	14 (6.9)	110 (54.2)	28 (13.8)	51 (25.1)	203 (100.0)		

Total mastectomy specimens with axillary lymph node dissection were examined for lymph nodal involvement and pTNM staging was done accordingly. Maximum cases (68; 54.4%) had no lymph node metastasis (N0); followed by N3 [Metastasis in 10 or more ipsilateral axillary lymph nodes (at least one larger than 2 mm) or metastasis in infraclavicular lymph nodes or involvement of level Ill lymph nodes- N3a; or metastasis in clinically detected internal ipsilateral mammary lymph node(s) in the presence of positive axillary lymph node(s); or metastasis in more than 3 axillary lymph nodes and in internal mammary lymph nodes with microscopic or macroscopic metastasis detected by sentinel lymph node biopsy but not clinically detected- N3b; or metastasis in ipsilateral supraclavicular lymph node(s)- N3c] with 22; 17.6% cases; followed by N2 [metastasis in 4-9 ipsilateral axillary lymph nodes, or in clinically detected ipsilateral internal mammary lymph node(s) in the absence of axillary lymph node metastasis]; and N1 [micrometastases; or metastases in 1 to 3 axillary ipsilateral lymph nodes; and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected] with 19 (15.2%) cases and 16 (12.8%) cases each.

Out of 22 N3 cases, 9 cases had metastasis in 10 or more ipsilateral axillary lymph nodes along with involvement of level III lymph nodes; 8 cases had 10 or more ipsilateral axillary lymph nodes involvement; while 4 cases had involvement of level III lymph nodes but number of positive axillary lymph nodes was less than 10. There was 1 case in which none of the axillary lymph nodes were involved, but metastatic deposits were seen in Level III lymph nodes.

Lymph node status was compared with the molecular subtypes. Maximum cases (38/ 68) with no lymph node metastasis had Luminal-B molecular profile.

Table 32- Status of lymph nodes in carcinoma breast (n=125):

Lymph node status	Number of cases	Percentage
N0	68	54.4
N1	16	12.8
N2	19	15.2
N3	22	17.6
Total	125	100.0

Table 33- Status of lymph nodes in carcinoma breast and their comparison with molecular subtypes (n=125):

Status of lymph nodes	Luminal-A (n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
N0	6	38	4	20	68 (54.4)	12.486	0.139
N1	1	8	3	4	16 (12.8)		
N2	2	10	5	2	19 (15.2)		
N3	0	16	3	3	22 (17.6)		
Total number of cases (n, %)	9 (7.2)	72 (57.6)	15 (12.0)	29 (23.2)	125 (100.0)		

Status of extranodal extension was observed for all cases with metastatic lymph nodes (57 in number). The area of invasion outside the lymph node capsule was included in the overall size of the lymph node metastasis and the size of the metastasis included the tumor cells alongwith the desmoplastic response. Extranodal extension was seen in 39/ 57; 19.2% cases.

A highly statistically significant association (p-value <0.001) was seen between the status of extranodal extension and the molecular subtypes of breast cancers. 24 out of 39 cases with extranodal extension belonged to luminal-B molecular subtype.

Treatment induced changes were noted in only 2 cases, seen as hemorrhage, necrosis, sclerosis and foamy macrophages.

Table 34- Status of extranodal extension (n=57):

Extranodal extension	Number of cases	Percentage
Present	39	68.4
Absent	18	31.6
Total	57	100.0

Table 35- Correlation of extranodal extension and molecular subtypes (n=57):

Extranodal extension	Luminal-A (n)	Luminal-B (n)	HER 2/ neu Enriched (n)	Triple negative (n)	Total number of cases (n, %)	Fisher's Exact Test Statistics	p-value
Present	1	24	8	6	39 (68.4)	228.694	<0.001
Absent	2	10	3	3	18 (31.6)		
Total number of cases (n, %)	3 (5.3)	34 (59.6)	11 (19.3)	9 (15.8)	57 (100.0)		

DISCUSSION

Breast cancer is a heterogeneous disease containing a variety of distinct clinical, morphological and molecular features and exhibiting a range of clinical characteristics and therapeutic implications. Classically, histopathological examination has been the gold standard for breast cancer diagnosis. However, a combination of both histopathology and immunohistochemistry is extremely helpful in guiding the lines of treatment and the prognosis. Immunohistochemistry is a convenient and an effective tool to reach an accurate diagnosis for invasive breast cancers.

The present 1 year prospective study (September 15, 2022 to September 14, 2023) on 'Correlation of histomorphological features with molecular subtypes of carcinoma breast' was conducted in the Department of Pathology, Dayanand Medical College and Hospital, Ludhiana. All cases of invasive, non-metastatic carcinoma breast undergoing immunohistochemistry testing for molecular subtyping were included in the study.

A total of 15,395 specimens were received during this study period, out of which 203 cases were of invasive breast carcinoma on which immunohistochemistry testing was done and were analysed with respect to light microscopic and immunohistochemical findings. We evaluated the distribution of molecular subtypes of carcinoma breast and their association and correlation with the epidemiological and histopathological factors like age, MBR grade, 'pT' (based on tumor size), Ductal Carcinoma In Situ (DCIS) including its architectural patterns and cytonuclear grade, Lobular Carcinoma In Situ (LCIS), necrosis, tumor extent including skin, nipple or skeletal muscle involvement, skin invasion, lymphatic and/ or vascular invasion (LVI), microcalcifications, margins, lymphocytic response at the advancing tumor margins, perineural invasion, lymph node status and extranodal extension. Statistically significant associations (p-value <0.05) were found between the molecular subtypes and MBR grade, necrosis, skin invasion, microcalcifications and extranodal extension.

This study comprised 203 cases of invasive breast carcinoma, out of which, most cases (99.5%) were females, only one case (0.5%) was of male breast cancer. This is comparable to the studies of Smriti Tiwari et al[103]. And Shet T et al[114]. who found 1.4% and 1.6% cases of male breast cancer respectively.

The age of patient presentation in our study ranged from 28 to 88 years, with maximum breast cancers occurring in post-menopausal females with age more than 50 years (64.5%) with the specific age group of 51-60 years, and a mean age of 56.3+/-12.4 years, alike the study of Rhodes et al[115]. in which alsothey observed the most common age group for invasive breast carcinomas to be more than 50 years with mean age of 64 years. In the study of Majid et al.[100], the maximum cases occurred in women with age more than or equal to 60 years. In another study, conducted by Sujoy Kumar De et al.[102], amongst the age ranges from 27 to 65 years, the median age was 49 years. Our age trends were in contrast to the study of Smriti Tiwari et al. [103], Mithila Bisht et al.[109], Vedashree MK et al.[116] and Chandrika Rao et al.[117]in which maximum cases belonged to age group of 41-50 years (i.e. perimenopausal and post-menopausal age groups). The impact of age was not very significant amongst our cases and its correlation with the molecular subtypes was not very significant (p-value 0.180).

Table 36- Comparison of age groups amongst various studies:

Study	Most common age group (cases, %)
Present study	51-60 years (28.1%)
Sujoy Kumar De et al.	41-50 years (36.7%)
Smriti Tiwari et al.	41-50 years (37.2%)
Mithila Bisht et al.	41-50 years (34.0%)
Chandrika Rao et al.	41-50 years (46.8%)

In our study, involvement of left breast (57.6% cases) was more, as compared to the right side (41.4% cases). Bilateral breasts were

involved only in1.0% cases. These trends were similar with the studies of Ankit Mittal et al.[112], Smriti Tiwari et al.[103] and Moses Ambroise et al.[118] who reported 69.0%, 68.6% and 59.2% cases in left breast, respectively. Geethamala K et al.[119] also reported slightly more cases in left breast than right. Whereas, in the study of Mithila Bisht et al.[109], there were 46.0% cases with right breast involvement, 43.0% cases with left breast involvement and 1.0% cases with bilateral breast involvements.

Table 37- Comparison of most common breast laterality amongst various studies:

Study	Most common breast laterality (cases, %)
Present study	Left (57.6%)
Ankit Mittal et al.	Left (69.0%)
Smriti Tiwari et al.	Left (68.6%)
Moses Ambroise et al.	Left (59.2%)
Geethamala K et al.	Left (50.0%)
Mithila Bisht et al.	Right (46.0%)

According to WHO classification 2019, maximum number of cases (89.2%) in our study belonged to Infiltrating Ductal Carcinoma (IDC), NOS followed by Invasive Lobular Carcinoma (3.9%); which is in concordance to studies conducted by Smriti Tiwari et al.[103], Elisabeth Christine Inwald et al.[104], Karangadan et al.[107] and Ankit Mittal et al.[112] who reported 90.0%, 81.9%, 90.0% and 66.0% cases of IDC, NOS; respectively. This was also the commonest histological subtype in the study of Soni et al.[110].

Table 38- Comparison of most common histological type amongst various studies:

Study	Most common histological type (cases, %)
Present study	IDC, NOS (89.2%)
Smriti Tiwari et al.	IDC, NOS (90.0%)
Elisabeth Christine Inwald et al.	IDC, NOS (81.9%)
Karangadan et al.	IDC, NOS (90.0%)
Ankit Mittal et al.	IDC, NOS (66.0%)

In the present study, there were 6 cases of mucinous carcinoma, 3 cases of metaplastic carcinoma and 1 case each of cribriform carcinoma, mixed IDC-NOS and invasive lobular carcinoma (85% lobular), encapsulated papillary carcinoma, invasive papillary carcinoma and solid papillary carcinoma.

All these histopathological diagnoses were then compared to the molecular subtypes and significant association was seen between the two (p-value <0.05). It was observed that 96 out of 178 IDC, NOS cases, 5 out of 8 Invasive Lobular Carcinoma cases, 5 out of 6 mucinous carcinoma cases, and cases of cribriform carcinoma, mixed IDC-NOS and invasive lobular carcinoma, encapsulated papillary carcinoma and solid papillary carcinoma had Luminal-B molecular profile; thus suggesting that Luminal-B molecular profile can present in various histomorphological subtypes. While all 3 metaplastic carcinoma cases had Triple negative molecular profile. Single case of invasive papillary carcinoma belonged to Luminal-A molecular subtype.

Thus, majority of the cases included in the study belonged to Luminal-B molecular subtype; representing 54.7% cases, which is compatible with the studies done by Swandari Paramita et al.[93], Ankit Mittal et al. [112] and Ayad Ahmad Mohammed et al.[111] in which the most prevalent intrinsic molecular subtype of breast cancer was found to be Luminal B (representing 42.4%, 28.0% and 43.7% cases; respectively). This is

even concordant with the study of Marina Ganadra-Cortes et al.[101], in which they compared the results obtained in the classification based on various Ki-67 and PR threshold values proposed by different authors and subclassified the Luminal A-like and the Luminal B-like (HER 2-negative) subtypes; and found Luminal-B (HER 2/ negative) cases to be more than Luminal-A cases in majority of the classifications (except the most recent one as proposed by Maisonneuve et al[120]).

HER 2/ neu enriched cases constituted 13.8 % cases of our study; which is similar to the study of Soni et al.[110], who reported 14.8% cases of HER 2/ neu enriched molecular subtype.

In the present study, 59.6% cases were immunonegative (0 or 1+) for HER 2/ neu; while 22.2% were immunopositive (3+). There were 18.2% cases with equivocal (2+) interpretation; out of which 17.2% cases underwent FISH testing for final evaluation of the case. While in the study of Soni et al.[110], 21.8% of cases were HER 2/ neu positive (3+), 9.2% of cases were equivocal (2+) and 69.0% cases were negative (0 or 1+). They considered equivocal results as negative. In the study of Ankit Mittal et al.[112], 30% cases were HER 2/ neu positive, 17% cases were HER 2/ neu negative and 8% cases were HER 2/ neu equivocal (2+), who were advised FISH testing but were lost to follow up.

The least common molecular subtype found in our study was Luminal-A (6.9% cases), which is in concordance with the study of Ankit Mittal et al.[112] and, in comparison with various other studies previously reported in literature like by Sujoy Kumar De et al.[102], Smriti Tiwari et al.[103] and Soni et al.[110] in which Luminal-A was the most common subtype.

Majority of other studies had a higher number of Luminal-A cases as compared to this study. While the cases of Luminal-B (54.2%) and Triple Negative (25.1%) molecular subtypes were higher in this study. The studies by Soni et al.[110] and Biswal et al.[121] showed 35% cases each, Bhagat Vasudha M et al. [122] showed 25.9% cases and Patil et al.[123] showed 19.9% cases as Triple negative respectively. While the study of Mithila Bisht et al.[109] showed only 9% cases of Triple negative molecular profile.

Table 39- Comparison of molecular subtypes amongst various studies:

Study	Molecular subtypes			
	Luminal-A (%)	**Luminal-B (%)**	**HER 2/ neu enriched (%)**	**Triple negative (%)**
Present study	6.9%	54.2%	13.8%	25.1%
Swandari Paramita et al.	7.6%	42.4%	39.1%	10.9%
Ankit Mittal et al.	22.0%	22.0%	25.0%	25.0%
Ayad Ahmad Mohammed et al.	28.0%	43.7%	20.9%	7.4%
Smriti Tiwari et al.	27.1%	25.7%	25.7%	21.4%

Out of 51 Triple negative breast cancer (TNBC) cases, 9.8% cases showed immunopositivity for CK5/6; thus indicating their Basal-like profile; which is coherent with the study of Asmerom Tesfamariam et al.[124], which had 10% cases of Basal-type molecular profile. Smriti Tiwari et al.[103] showed 15.7% cases and Soni et al.[110] showed 17% Basal-type cases, respectively. A significantly higher number of Basal-like cases (58.7%) were recorded in the study of Yunita Setyawati et al. [108].

We also studied expressions of GATA-3 and SOX-10 in all TNBC cases. GATA-3 immunopositivity was seen in 38 out of 51 TNBC cases, while 17 out of 51 cases came showed immunopositivity for SOX-10. Combined immunopositivity of both SOX-10 and GATA-3 was seen 12 cases. While, there were 2 cases, in which both SOX-10 and GATA-3 were immunonegative, but CK 5/6 showed immunopositivity.

Hence, SOX-10 when combined with GATA-3 expression, served as an important diagnostic marker for TNBC cases in our study.

In the present study, according to the severity of invasive breast cancers, 56.7% had Modified Bloom Richardson (MBR) Grade 2followed by Grade 3 (34.0%) and Grade 1 (9.4%). This was in concordance with the study of Smriti Tiwari et al.[103] in which 60% cases belonged to Grade 2, 22.9% cases belonged to Grade 3 and 17.1% cases belonged to Grade 1. Also, in the study of Mithila Bisht et al.[109] and Ankit Mittal et al.[112], majority cases belonged to Grade 2 (73% and 56%), respectively. This is consistent with numerous other Indian researches, such as those conducted by Soni et al.[110], Vedashree MK et al. (Chennai)[116], Geethamala K et al. (Bangalore)[119], Bhagat Vasudha M et al. (Surat)[122], Kanchan et al. (U.P.)[125], and Suvarchala et al. (Chennai)[126].

Majority of the Grade 2 tumors belonged to Luminal-B molecular subtype and a statistically significant association was found between the MBR grade and the molecular subtypes (p value ≤0.001).

It was found that majority of cases of Triple negative molecular subtype (35 out of 51) were histological grade 3 tumors; similar to studies conducted by Mithila Bisht et al.[109] and Geethamala K et al.[119]. This suggests the tumor aggressiveness of this molecular subtype.

Table 40- Comparison of MBR grades amongst various studies:

Study	MBR grades		
	1 (%)	2 (%)	3 (%)
Present study	9.4%	56.7%	34.0%
Smriti Tiwari et al.	17.1%	60.0%	22.9%
Mithila Bisht et al.	16.0%	73.0%	11.0%
GeethamalaK et al.	19.0%	54.0%	27.0%
Vedashree MK et al.	9.6%	72.6%	17.8%

In the present study, the tumors (mastectomy/ breast conservation surgery (BCS)/ excision/ lumpectomy specimens; but not trucut biopsies) were classified according to the pTNM classification, out of which maximum (68.8%) cases belonged to T2 which is concordant with the study of Mithila Bisht et al.[109] and Ahmad et al.[127], in which maximum cases were T2 with 52% and 44.2% cases, respectively. Our findings also align with earlier Indian research conducted in Chennai by Vedashree MK et al.[116], in Cuttack by Biswal et al.[121], and Suvarchala et al.[126]. But, in the study of Smriti Tiwari et al.[103], 61.4% were T3, 37.2% were T2 and only 1.4% cases were T1. Adendaya et al.[128] study from a Western nation revealed that 71% of instances of breast cancer had a size of less than 2 cm i.e. T1. This can be explained by the dearth of breast cancer screening programs in our nation and, conversely, in the western countries, as well as the absence of knowledge about breast cancer.

Table 41- Comparison of 'pT' amongst various studies:

Study	'pT' (based on tumor size)			
	pT1	pT2	pT3	pT4
Present study	14.9%	68.8%	13.6%	2.6%
Mithila Bisht et al.	23.0%	52.0%	25.0%	-
Ahmad et al.	7.5%	44.2%	41.7%	6.7%
Smriti Tiwari et al.	1.4%	37.2%	61.4%	-

In the present study, DCIS component was noted in 24.6% cases; 13.8% of which had intermediate grade and 11.3% had high grade DCIS component. Soni et al.[110] reported 22.3% cases of co-existing intraductal component with IDC. P.A. van Luijt et al. (Netherlands) [129] in his screening programme on 4232 women with a diagnosis of DCIS observed 50.9% high grade DCIS, 31.4% intermediate grade DCIS, and 17.7% of low grade DCIS component. Soni et al.[110] reported 22.3% cases of co-existing intraductal component with IDC.

Comedo pattern was seen in maximum number of cases (22.7%) followed by solid pattern (21.7%). Lobular carcinoma in situ (LCIS) was seen in 1 case (0.5%). Maximum breast cancer cases with ductal component belonged to Luminal-B molecular subtype (28 cases) followed by HER 2/ neu enriched type (11 cases).

In the present study, necrosis was seen in 26.1% cases; whereas, Soni et al.[110] and Ahmad et al.[127] documented tumor necrosis in 46.2% and 63.3% cases, respectively. The study of AA Thike et al.[130] on TNBCs showed presence of necrosis in 98.0% cases.

Our study showed a statistically significant association between the status of necrosis and the molecular subtypes of carcinoma breast with a p-value of <0.05.

In the present study, status of skin invasion was noted [wherever applicable; i.e. in mastectomy and breast conservation surgery (BCS) specimens] and was found to be present only in 4.2% of the total cases. There were 4 cases with ulceration of the overlying skin and 2 cases

with dermal involvement. Epidermis was free of tumor in all cases included in the study. Thaer Khoury et al.[131] compared the survival analyses between a subset (n = 38, study cohort) and cases (n = 38, matched cohort) that did not have skin ulceration. After that, cases (n=80) were divided into stages I, II, or III without assistance from skin ulceration. Analysis was done on overall survival and disease-free survival. More often than individuals with smaller tumors, people with larger tumors tended to present with distant metastases.

In our study, a highly statistically significant correlation was seen between the status of skin invasion and the molecular subtypes of carcinoma breast with p-value of <0.001.

In our study, lymphatic and / or vascular invasion was seen in 20.2% cases. Soni et al.[110] found lymphovascular invasion (LVI) in 32.4% cases, while Ankit Mittal et al.[112] reported LVI in 47% cases. Ahmad et al.[127] studied the status of vascular invasion and found it to be present in 35.8% cases.

Microcalcifications were noted in 18.7%of our study cases and formed a significant association when compared with the molecular subtypes ($p<0.05$). V. Bouropoulou et al.[132] in their study, observed a higher incidence of microcalcifications, accounting for 41.0% of total cases. In the study of Angelica Selim et al.[133], microcalcifications were limited to malignant components in 31.0% cases and to benign components in 34.0% cases; and they were present in both in 34.0% cases. Though not all researches agree, calcifications may also be linked to tumor invasion into the lymphatic system. According to Tabar et al.[134], compared to stellate lesions without calcifications, the presence of casting calcifications was associated with a 3.3-fold higher incidence of positive lymph node status. Literature also suggests a strong association between the presence of calcifications and HER 2/ neu overexpression; although, in our study, majority cases belonged to Luminal-B molecular subtype.

In the present study, majority cases had infiltrating tumor margins (96.6% cases). While pushing margins were seen in only 6 (3.0%) cases. There was 1 case (0.5%) with pushing and focally infiltrating margins.

In the study of AA Thike et al.[130] on TNBCs, there were 84.0% cases with infiltrating tumor margins and 16.0% cases with pushing margins. Significant lymphocytic response at the advancing tumor margins was noted in37.4% cases (mild in 27.6% cases, moderate in 6.4% and marked lymphocytic response in 3.4% cases). Whereas, Sreeja Jayalakshmi et al.[135] observed high grade peritumoral infiltrate in 66.7% cases.

In the present study, perineural invasion was noted in only 4.9%cases; alike the study of Soni et al.[110] who documented 6.1% cases with perineural invasion. While, the study of Priyanka Narayan et al.[136], reported 15.6% cases with perineural invasion.

Total mastectomy specimens with axillary lymph node dissection were examined for lymph nodal involvement and pTNM staging was done accordingly. Maximum cases (54.4%) had no lymph node metastasis (N0). Lymph node metastasis was seen in45.6% cases in which maximum were N3 (17.6%) followed by N2 (15.2%) and N1 (12.8%). In the study of Yunita Setyawati et al.[108] also, frequency of negative lymph node status (59.9% cases) was higher than positive lymph node status (40.1% cases). Mithila Bisht et al.[109] reported 37% cases with lymph node metastasis in their study on 100 cases of Infiltrating Duct Carcinoma. Bhagat Vasudha M et al.[122] reported 53.4% cases with axillary lymph node metastasis; while Soni et al.[110] and Ankit Mittal et al.[112] reported 55.2% and 58.0% cases of lymph node metastasis, respectively. Smriti Tiwari et al.[103] in their study, compared lymph node status with the tumor size and found no lymph node involvement in T1, while in T2 and T3, 38.5% and 61.5% cases had positive lymph node status respectively. They also compared the lymph node status with the MBR grade and observed that, 19.3% of cases with positive lymph node status belonged to grade 1, whereas 57.7% and 23.0% cases with positive lymph node status belonged to grade 2 and grade 3. Ahmad et al.[127] also studied distribution of lymph node status and found maximum cases to be N1 (27.1%), followed by N0, N2 and N3.

The highest number of lymph node metastasis was observed in Luminal-B molecular subtype (16.7%) followed by HER 2/ neu enriched (5.4%), Triple negative (4.4%) and Luminal-A (1.5%) molecular subtypes. Ankit Mittal et al.[112] also observed maximum cases of lymph node positivity in Luminal-B molecular subtype (19.0%), followed by Triple negative (17.0%) and HER 2/ neu enriched (13.0%) molecular profiles.

Table 42- Comparison of nodal status amongst various studies:

Study	Positive	Negative
Present study	45.6%	54.4%
Yunita Setyawati et al.	40.1%	59.9%
Mithila Bisht et al.	37.0%	63.0%
Smriti Tiwari et al.	74.3%	25.7%
Ahmad et al.	74.8%	25.2%

We observed status of extranodal extension for all cases with metastatic lymph nodes (57 in number). Extranodal extension was seen in 19.2% cases. This is in contrast to the study of Ahmad et al.[127], in which they found extranodal spread in 70% cases in which lymph nodes were positive.

Our study had a highly statistically significant association (p-value <0.001) between the status of extranodal extension and the molecular subtypes of breast cancers. 24 out of 39 cases with extranodal extension belonged to luminal-B molecular subtype.

SUMMARY AND CONCLUSION

This study was conducted in Dayanand Medical College and Hospital, Ludhiana, over a period of one year (September 15, 2022 to September 14, 2023). A total of 203 histologically diagnosed invasive breast cancers were examined with respect to their immunohistochemical findings.

The following features were highlighted in this study:

- During the study period, a total of 15,395 specimens were received for histopathological examination in our department. Out of these, 203 cases of carcinoma breast were analysed with respect to light microscopy and immunohistochemical findings.
- The age of patients in our study ranged from 28 to 88 years, with a mean age of 56.3+/-12.4 years. Maximum invasive breast cancers occurred in 5th decade of life.
- Infiltrating Duct Carcinoma, NOS formed the largest histological group with 181 cases (89.2%); out of which 3 cases (1.5%) had medullary pattern. Invasive Lobular Carcinomas comprised 8 cases (3.9%). There were 6 cases of mucinous carcinoma, 3 cases of metaplastic carcinoma and 1 case each of cribriform carcinoma, mixed IDC-NOS and invasive lobular carcinoma (85% lobular), encapsulated papillary carcinoma, invasive papillary carcinoma and solid papillary carcinoma.
- The most commonly found molecular subtype was Luminal-B (54.2% cases), followed by Triple negative (25.1%), HER 2/ neu enriched (13.8%); and Luminal A(6.9%).
- Amongst 14 (6.9%) Luminal-A cases; all had an Allred score of 8/8 for ER, while 10 out of 14 cases had a score of 8/8 for PR. There was 1 case each of 0/8, 3/8, 5/8 and 6/8. In case of immunonegative PR (0/8), Ki-67 proliferation index was estimated to be only 8% in the highest proliferating areas (i.e. less than 14%).
- Amongst 110 (54.2%) Luminal-B cases, a range of 3/8 to 8/8 was observed, with majority of them having an Allred score of

8/8. While for PR, Allred scores ranged from 0/8 to 8/8. A higher value of Ki-67 proliferation index was observed (i.e. more than or equal to 14%) with a range of 18% to 90% in the highest proliferating areas.

- For HER 2/ neu immunostaining, 121 cases (59.6%) were interpreted as immunonegative (0 or 1+) for HER 2/ neu; while 45 cases (22.2%) were immunopositive (3+) for HER 2/ neu. There were 37 cases (18.2%) with equivocal (2+) interpretation; out of which 35 underwent FISH testing for final evaluation of the case, out of which 6 cases turned out to be positive.
- Amongst 51 (25.1%) cases of Triple negative molecular subtype, all cases had negative immunostaining for ER, PR and HER 2/ neu with Ki-67 having a range of 25% to 95% in the highest proliferating areas.
- Immunopositivity of CK 5/6 was seen in 20 out of 51 cases of Triple negative breast cancers (TNBC), thus indicating their basal-like profile.
- Expressions of GATA-3 and SOX-10 were also studied in all TNBC cases. GATA-3 immunopositivity was seen in 38 out of 51 TNBC cases, while 17 out of 51 cases came showed immunopositivity for SOX-10. Combined immunopositivity of both SOX-10 and GATA-3 was seen 12 cases. While, there were 2 cases, in which both SOX-10 and GATA-3 were immunonegative, but CK 5/6 showed immunopositivity. Hence, SOX-10 when combined with GATA-3 expression, served as an important diagnostic marker for TNBC cases in our study.
- Majority tumors had MBR Grade 2, constituting 56.7% cases, followed by Grade 3 (34.0%) and Grade 1 (9.4%). Majority of the grade 2 tumors (64.3%) belonged to Luminal-B molecular subtype with a highly significant p-value of <0.001.
- Considering pathological T category, maximum cases (68.8%) belonged to T2; followed by T1 (14.9%), T3(13.6%) and T4

(2.6%). Majority of T2 cases belonged to molecular subtype Luminal B.

- DCIS component was noted in 24.6% cases; majority of which had intermediate grade followed by high grade DCIS component. Comedo pattern was seen in maximum number of cases (22.7%) followed by solid pattern (21.7%). Lobular carcinoma in situ (LCIS) was seen only in 1 case (0.5%). Maximum breast cancer cases with ductal component belonged to Luminal-B molecular subtype (28 cases) followed by HER 2/ neu enriched type (11 cases).
- Necrosis was seen in 26.1% cases; out of which majority cases were Luminal-B type followed by Triple negative molecular subtype. A statistically significant association was found to be present between the status of necrosis and the molecular subtypes of carcinoma breast with a p-value of <0.05.
- Skin invasion was seen in only 4.2% of the total cases. There were 4 cases with ulceration of the overlying skin and 2 cases with dermal involvement. Epidermis was free of tumor in all cases included in the study. Thus, no case of Paget disease or pagetoid spread was noted. A highly statistically significant correlation was seen between the status of skin invasion and the molecular subtypes of carcinoma breast with p-value of <0.001.
- Lymphatic and/ or vascular invasion (LVI) was seen in20.2%cases; majority of which belonged to molecular subtype Luminal-B.
- Microcalcifications were noted in 18.7% cases and had a significant association when compared with the molecular subtypes (p<0.05). Maximum cases having microcalcifications belonged to Luminal-B molecular subtype.
- Maximum carcinoma breast cases had infiltrating margins (96.6% cases); majority of which belonged to Luminal-B type. While pushing margins were seen in only 3.0%cases. There was 1 case (0.5%) with pushing and focally infiltrating margins.

- Significant lymphocytic response at the advancing tumor margins was noted in 37.4%cases; majority of which belonged to molecular subtype Luminal-B. Lymphocytic response was mild in 27.6% cases, moderate in 6.4% cases and marked in 3.4% cases.
- Perineural invasion was noted in only 4.9% cases; majority of which belonged to Luminal-B type on immunohistochemistry.
- Maximum cases (54.4%) had no lymph node metastasis (N0); followed by N3 (17.6%), N2 (15.2%) and N1 (12.8%) cases. Maximum cases with no lymph node metastasis had Luminal-B molecular profile.
- Extranodal extension was seen in 19.2% cases. A highly statistically significant association (p-value <0.001) was seen between the status of extranodal extension and the molecular subtypes of breast cancers. Maximum cases with extranodal extension belonged to luminal-B molecular subtype.

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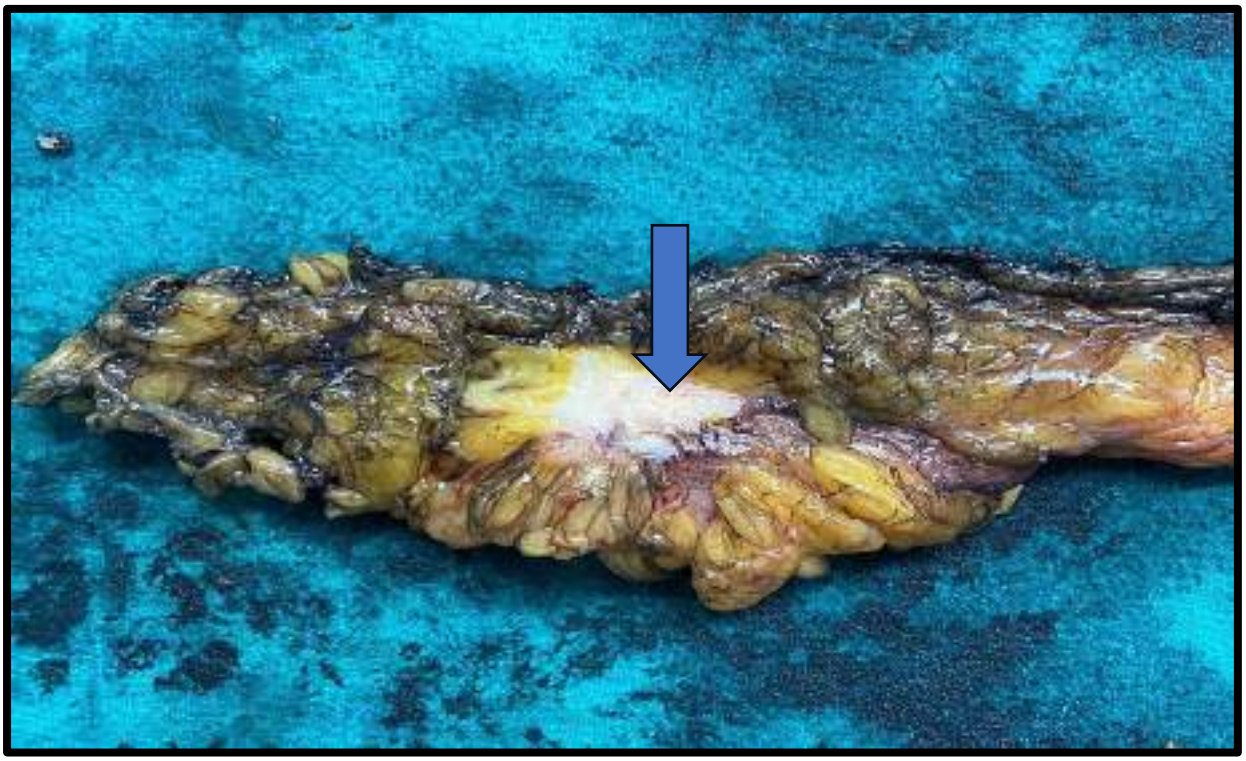
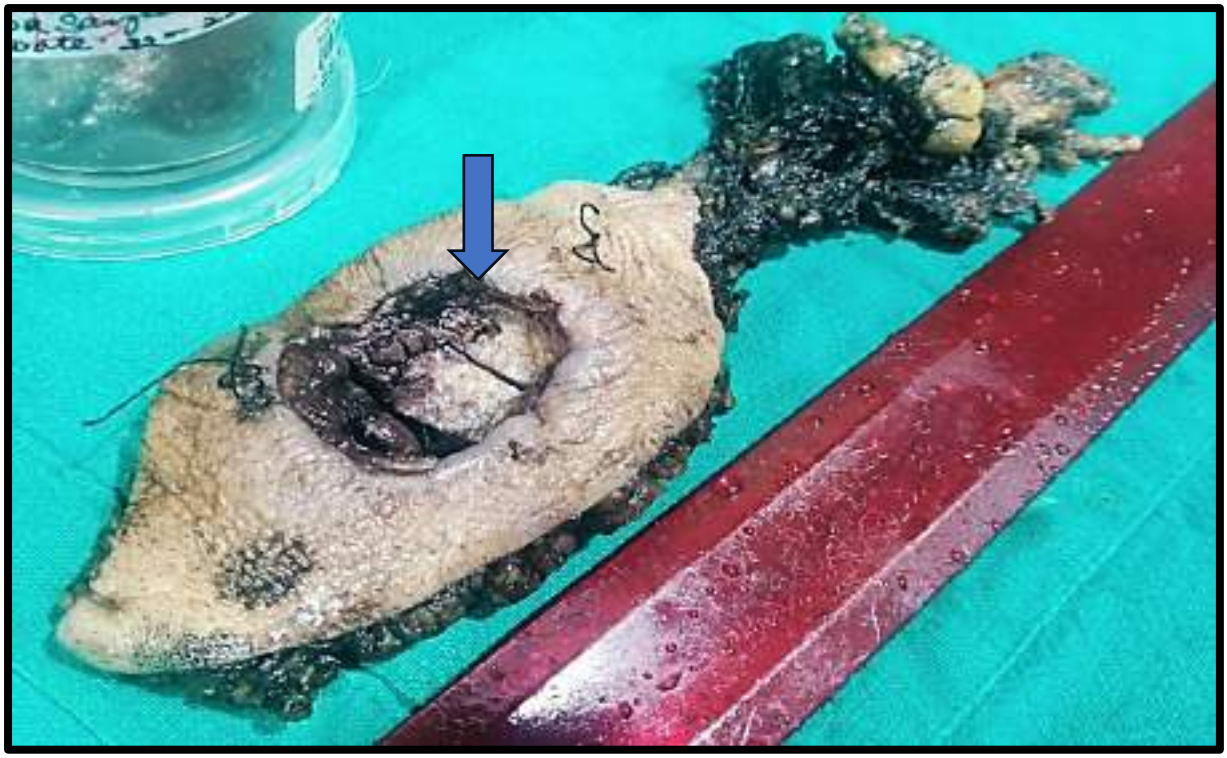
Picture 1- Photograph showing presence of tumor (arrows) in total mastectomy specimen.

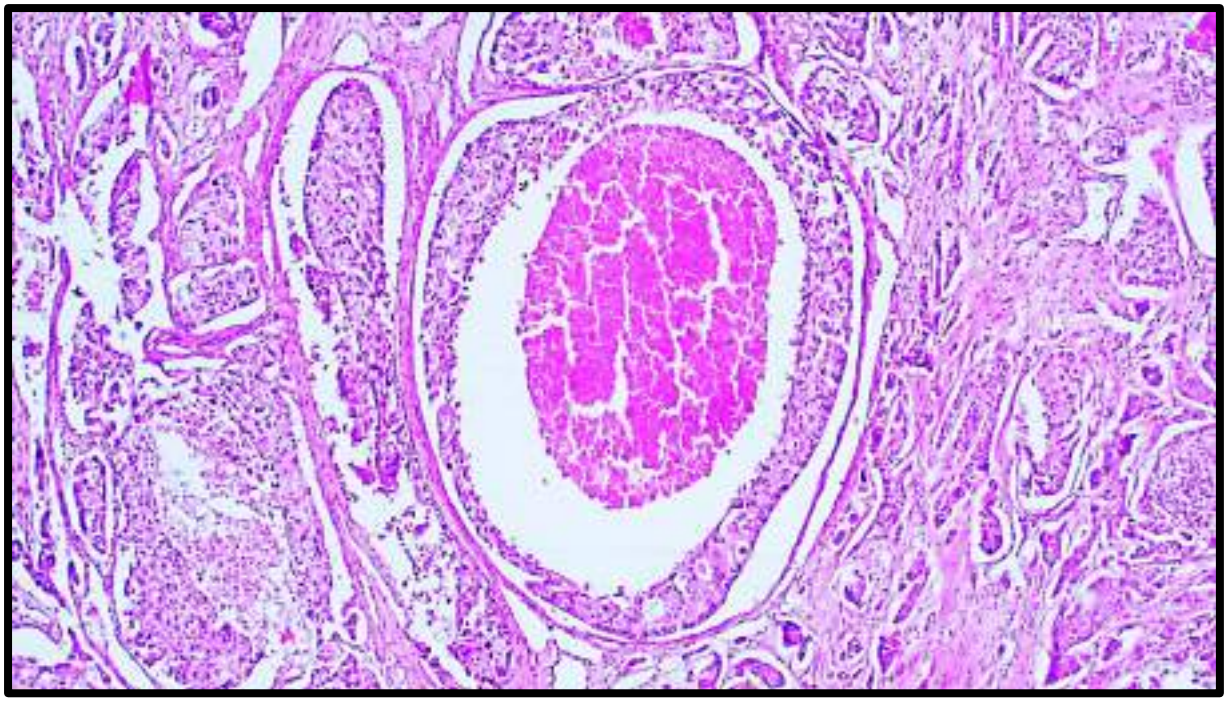


Picture 2- Photograph showing presence of tumor (arrow) measuring 2.2X1.5X1.2 cms. It lies at a distance of 0.8 cms from the surgical resected (inked) margin.

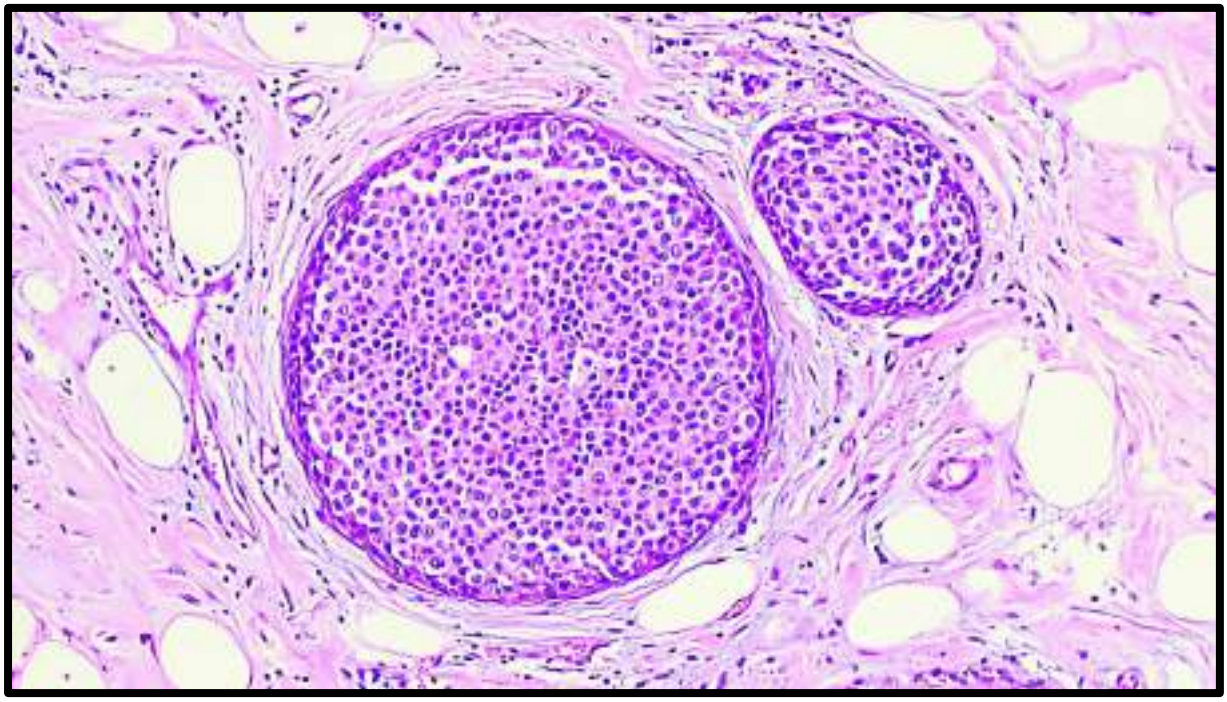


Picture 3- Photograph of mastectomy specimen showing skin ulceration (arrow) involving the nipple- areola complex completely, thus making it as T4b.

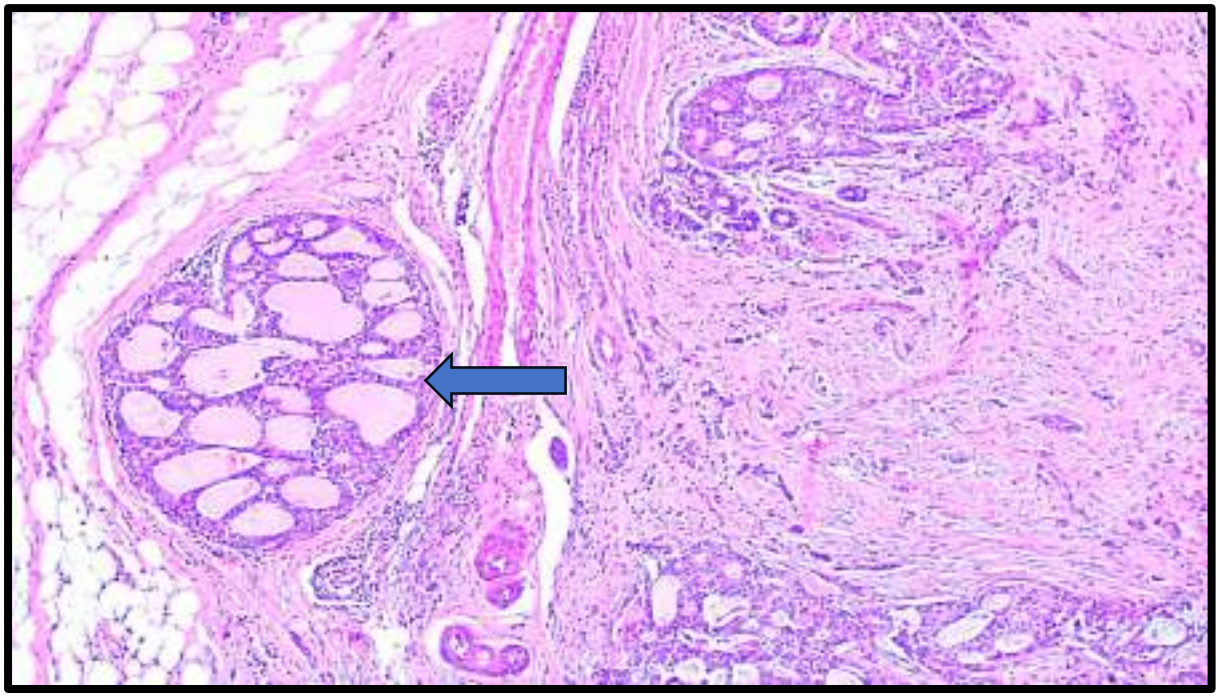
Picture 4- Photograph showing mastectomy specimen with axillary lymph nodes containing grey white tumor (arrows).



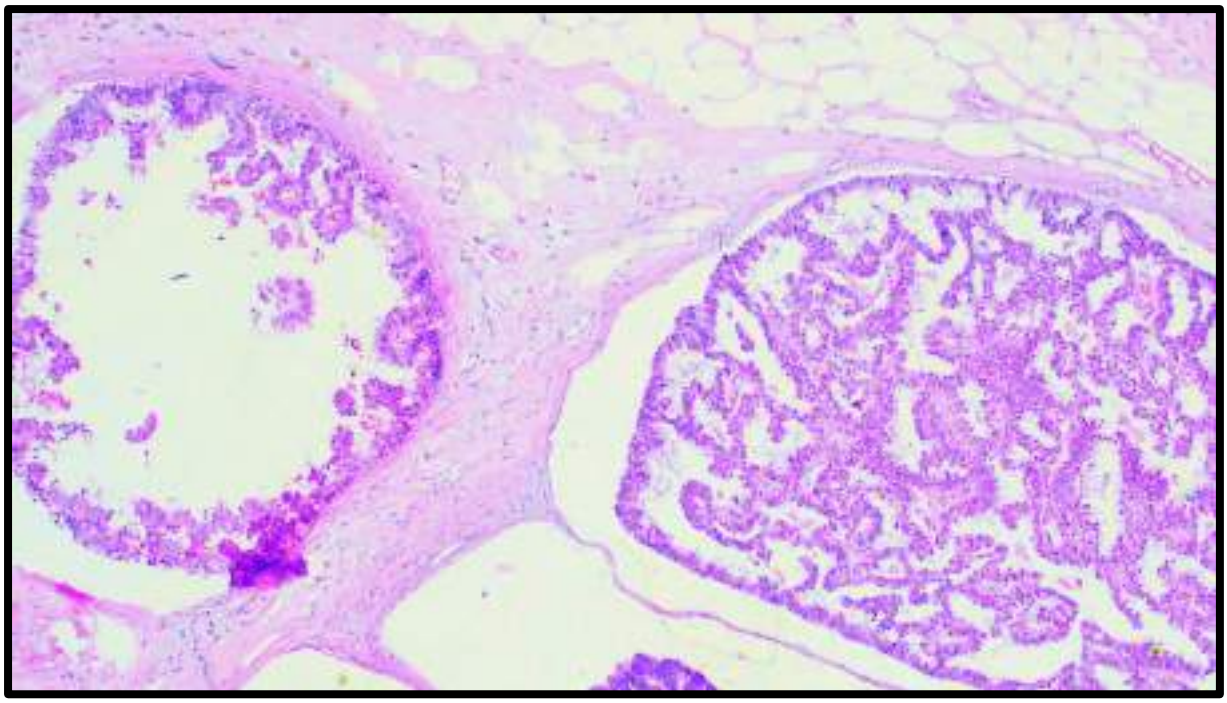
Picture 5- Photomicrograph of Ductal carcinoma in situ (DCIS) component- Comedo type, showing necrosis within the centre of the duct (H&E, 100X)



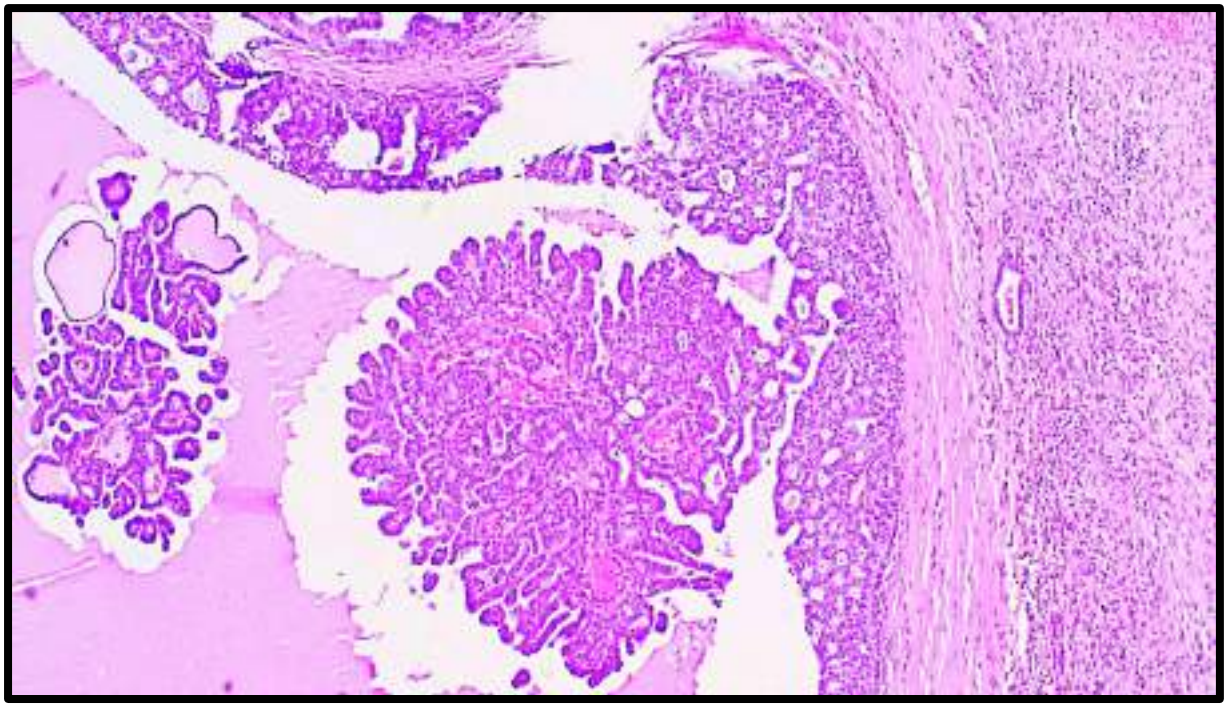
Picture 6- Photomicrograph of Ductal carcinoma in situ (DCIS) component- Solid type, showing proliferation of sheets of monomorphic, cohesive cells that are filling the ducts completely (H&E, 100X)



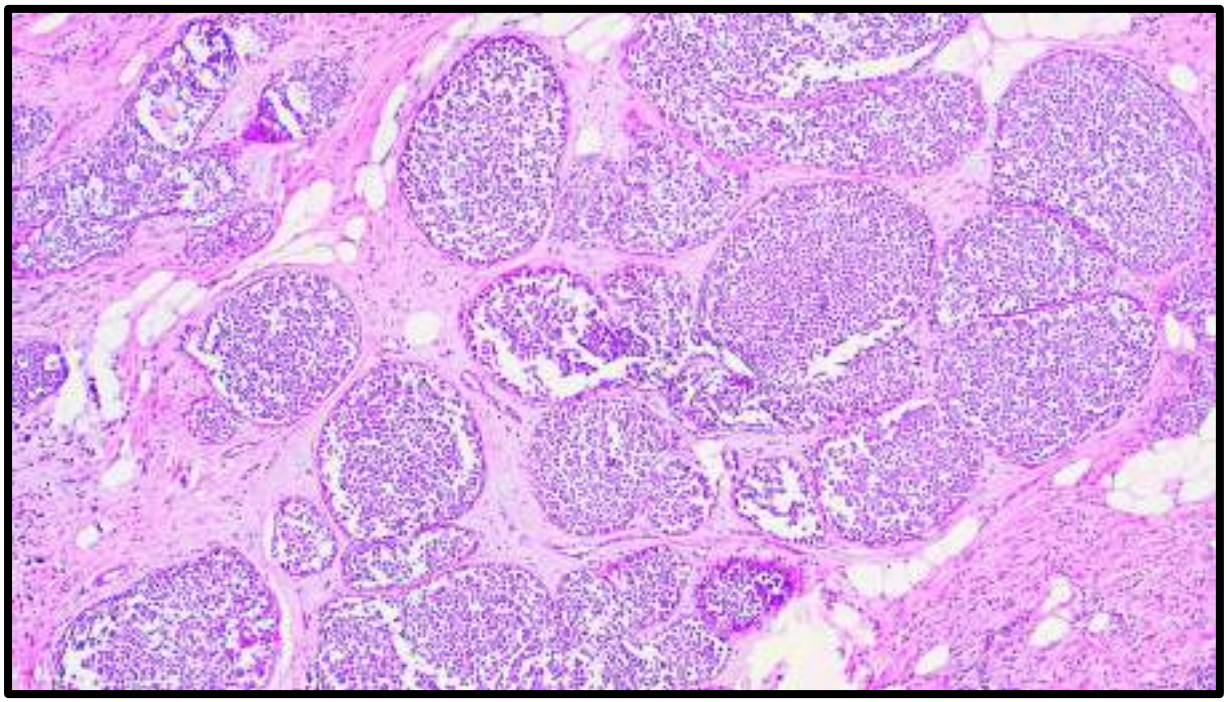
Picture 7- Photomicrograph of Ductal carcinoma in situ (DCIS) component- Cribriform type, showing presence of cohesive tumor cells perforated by variably-sized circular spaces, creating a sieve-like appearance (arrow) (H&E, 100X)



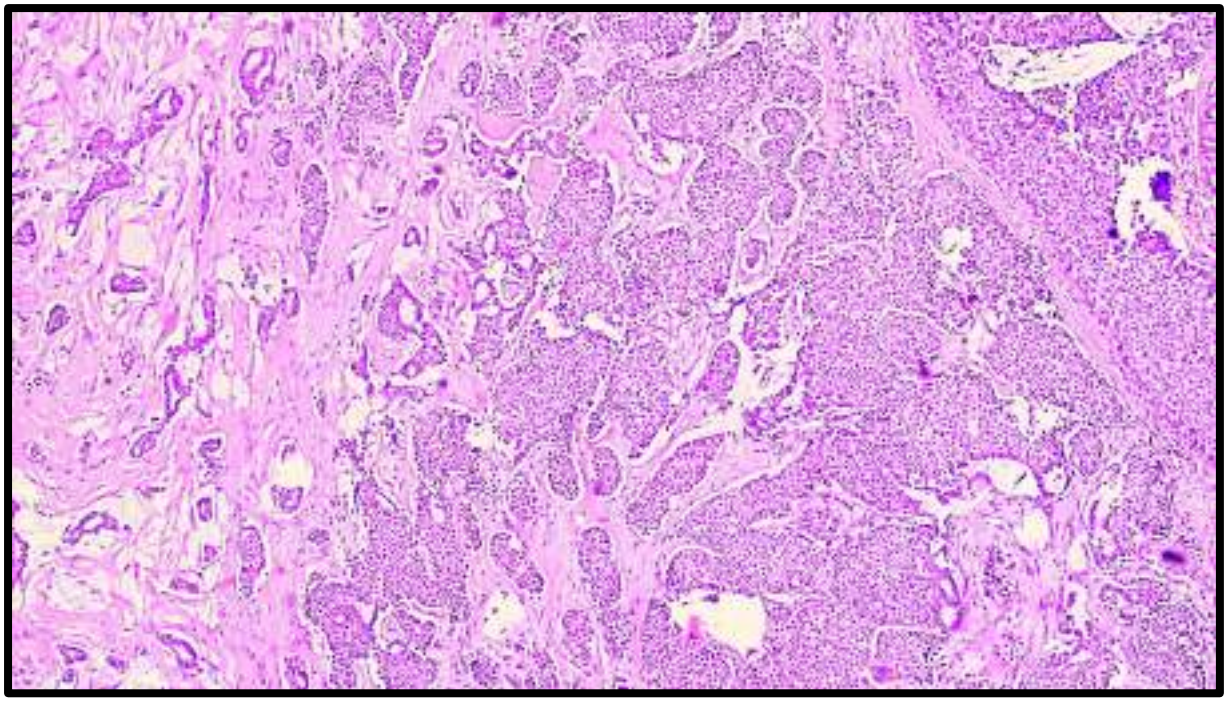
Picture 8- Photomicrograph of Ductal carcinoma in situ (DCIS) component- Micropapillary type, showing bulbous expansion at the tips (H&E, 40X)



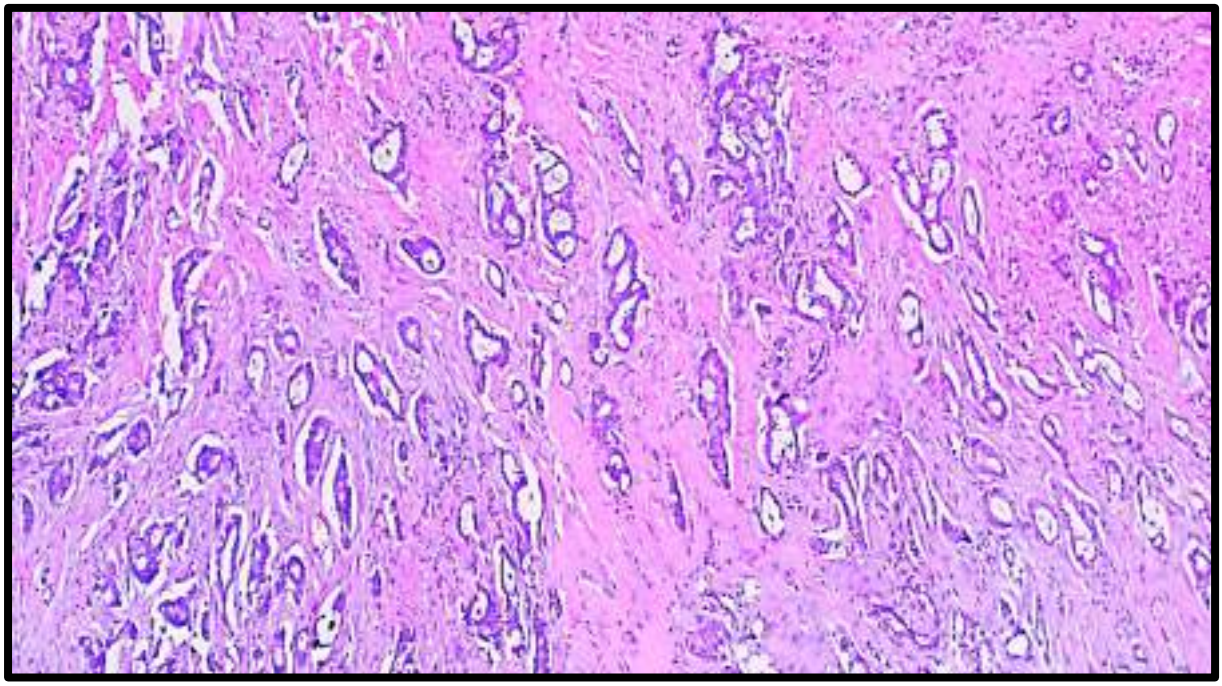
Picture 9- Photomicrograph showing Ductal Carcinoma in situ (DCIS component)- Papillary type, showing papillary projections with fibrovascular cores (H&E, 40X)



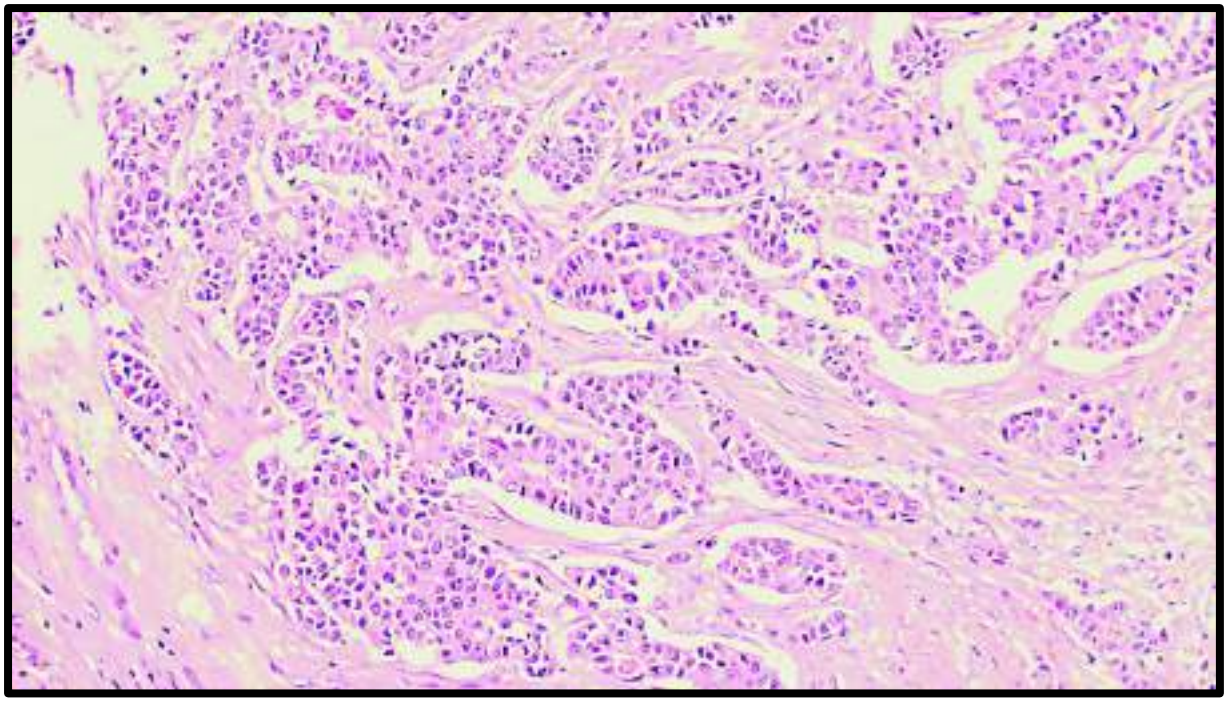
Picture 10- Photomicrograph showing marked expansion of the lobular units by tumor cells- Lobular Carcinoma in situ (LCIS) (H&E, 100X)



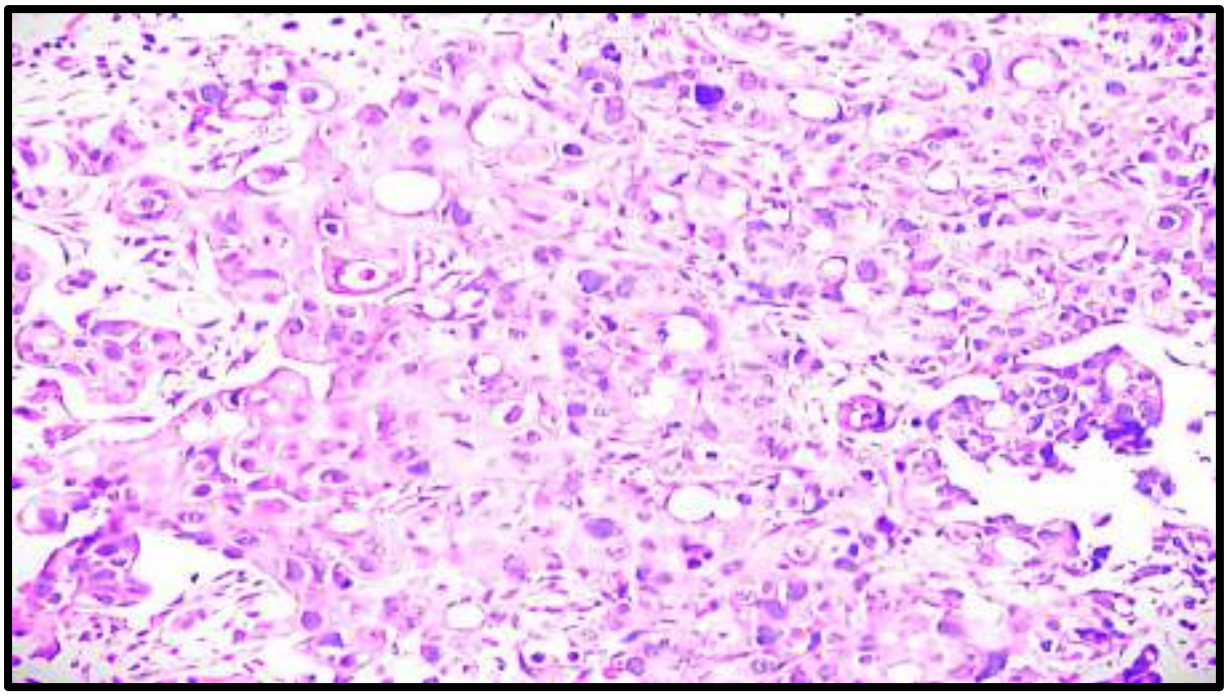
Picture 11- Photomicrograph of Infiltrating Duct Carcinoma (IDC), NOS showing clusters and nests of tumor cells, separated by sclerotic stroma (H&E, 40X)



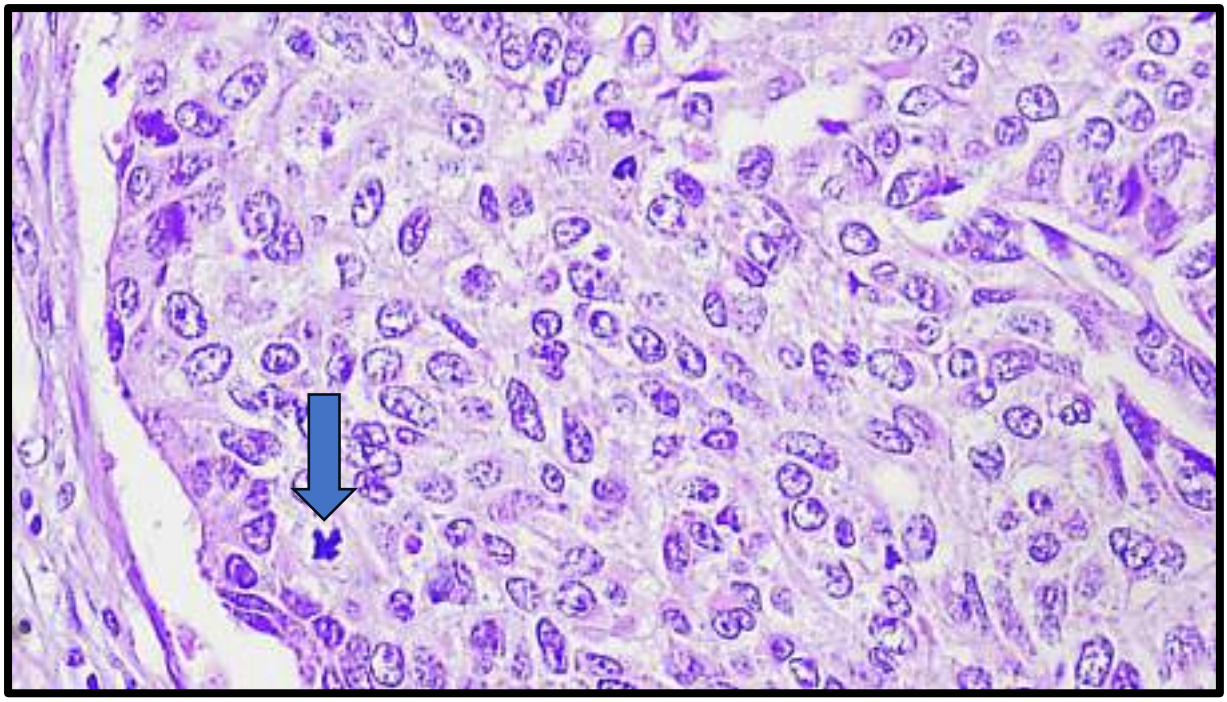
Picture 12- Photomicrograph showing Modified Bloom Richardson (MBR) grade 1 tumor, showing tubule formation in majority (>75%) of the tumor, mild nuclear pleomorphism and no significant mitosis (≤5/ 10 hpf) (H&E, 40X)



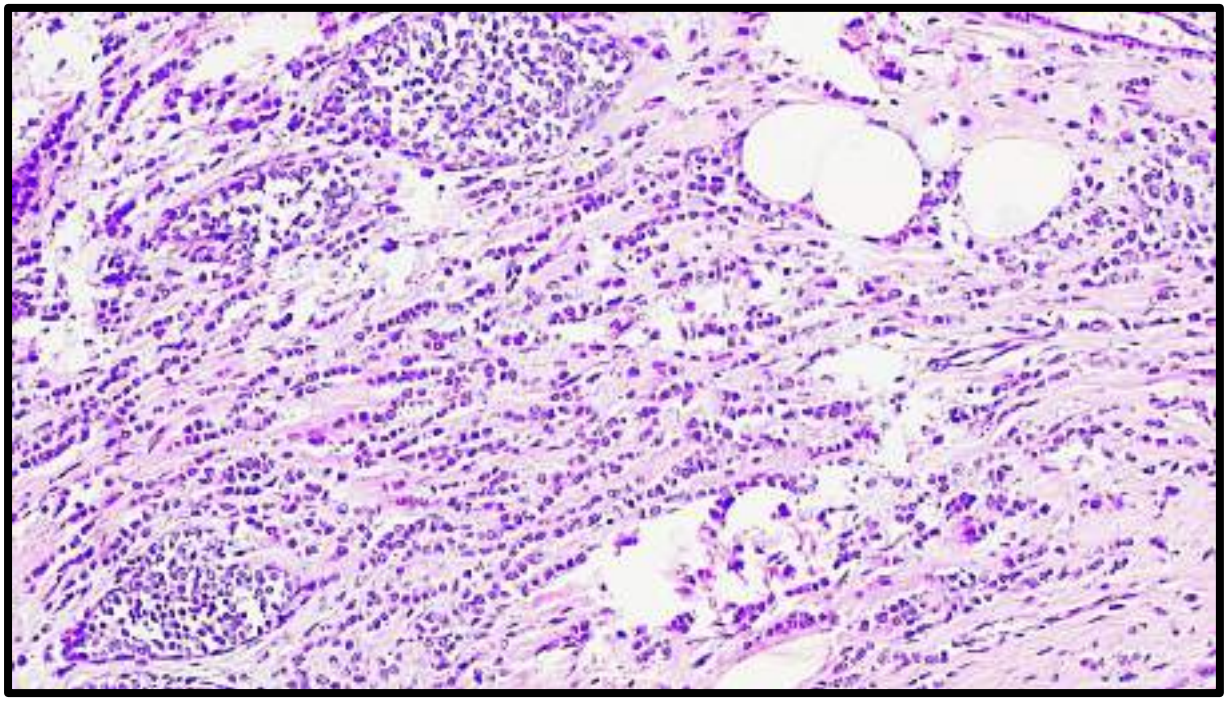
Picture 13- Photomicrograph showing Modified Bloom Richardson (MBR) grade 2 tumor, showing moderate degree (10-75%) of tubule formation, moderate nuclear pleomorphism and mitosis in the range of 6-10/ 10 hpf (H&E, 100X)



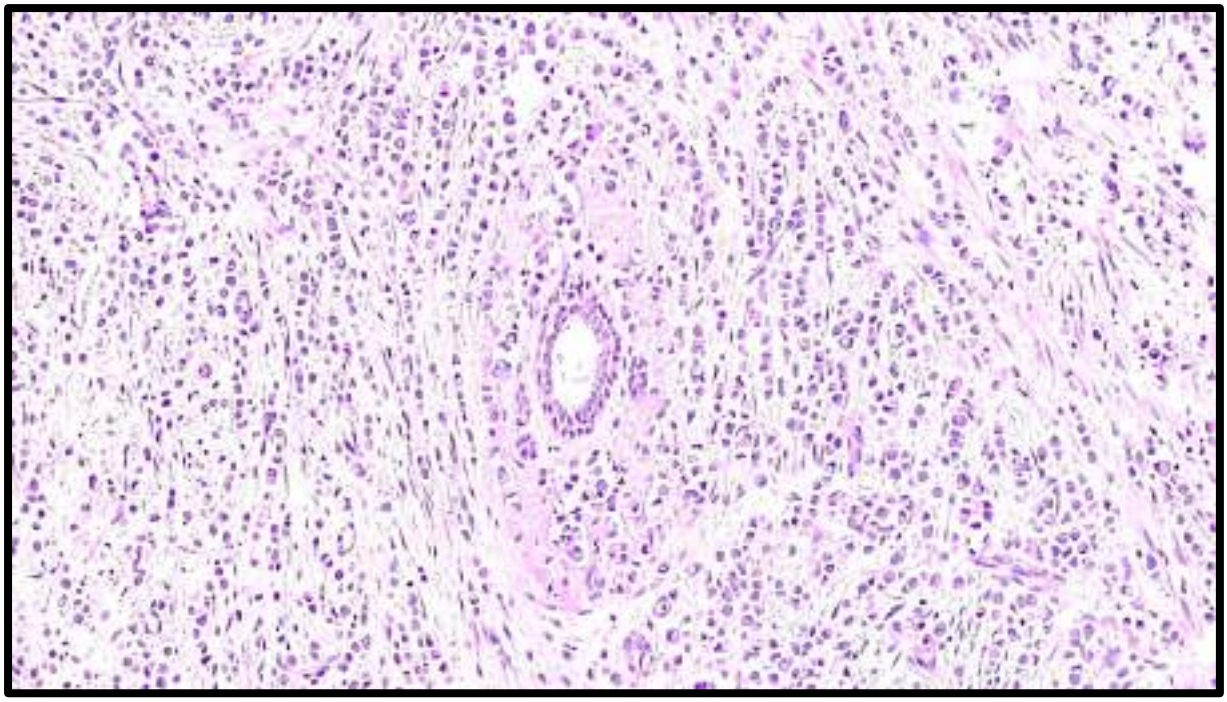
Picture 14- Photomicrograph showing Modified Bloom Richardson (MBR) grade 3 tumor, displaying <10% tubule formation, marked nuclear pleomorphism and mitosis in the range of ≥10/ 10 hpf (H&E, 40X)



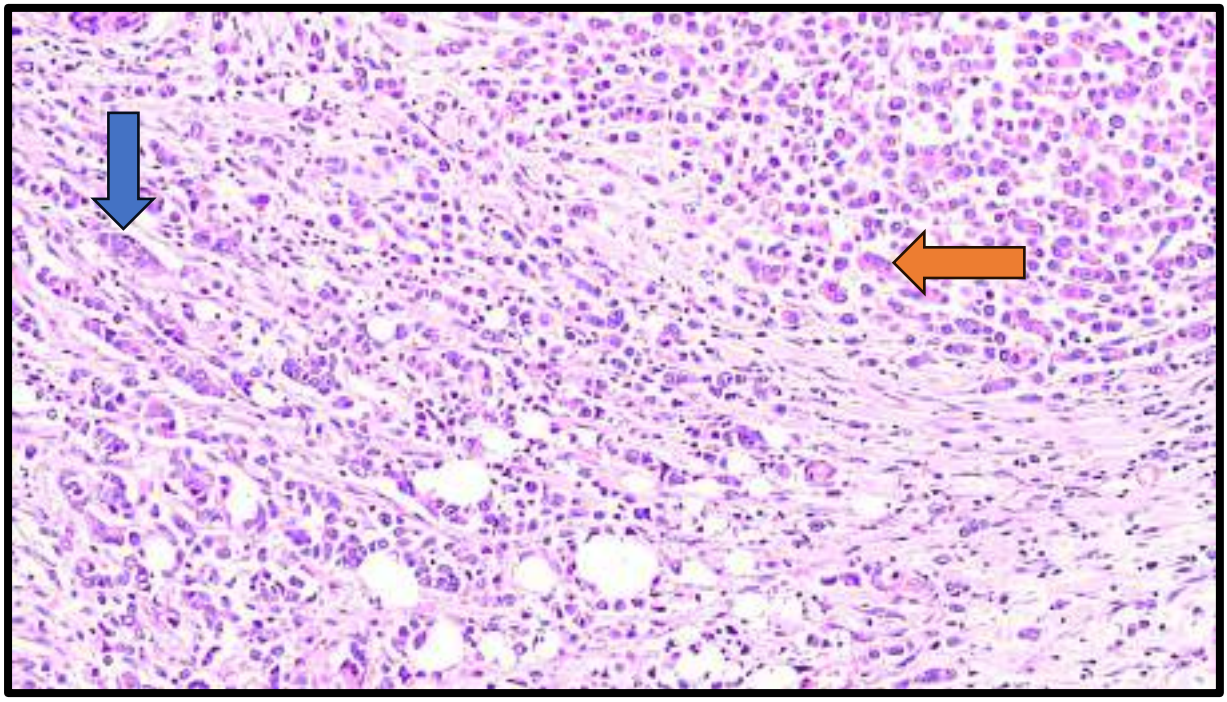
Picture 15- Photomicrograph showing presence of atypical mitotic figures (arrow) (H&E, 400X)



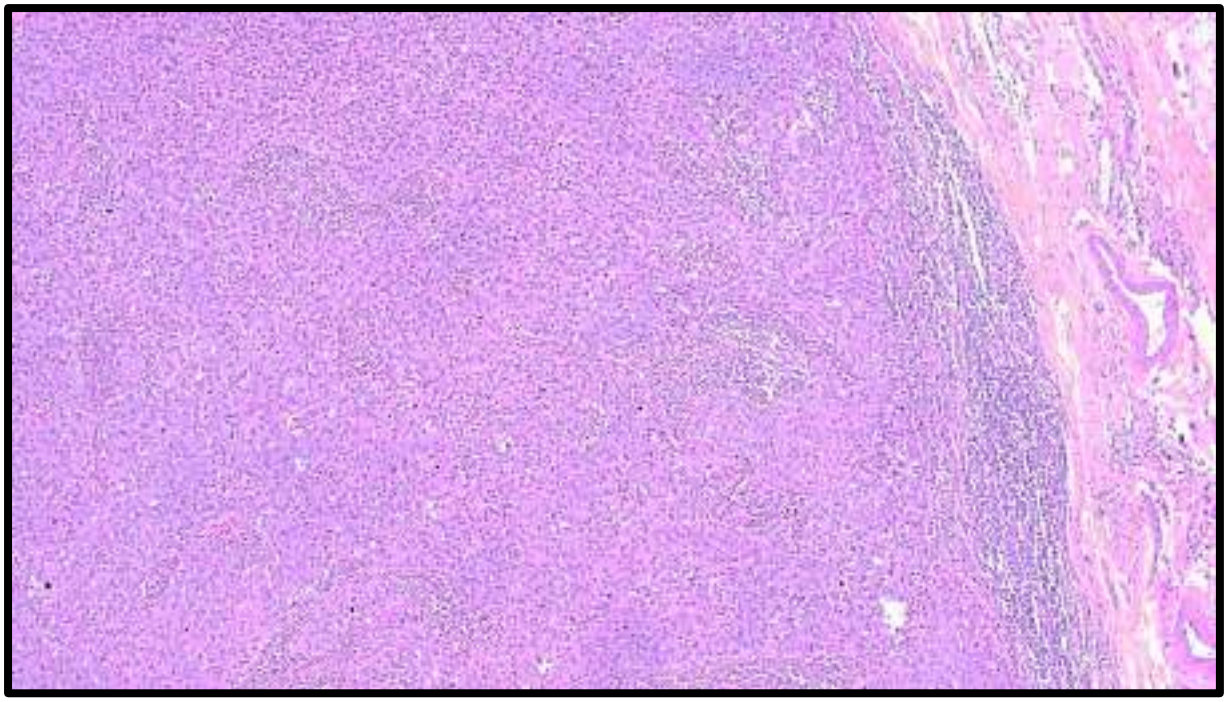
Picture 16- Photomicrograph of Invasive Lobular Carcinoma (ILC) showing Indian file pattern of tumor cells (H&E, 100X)



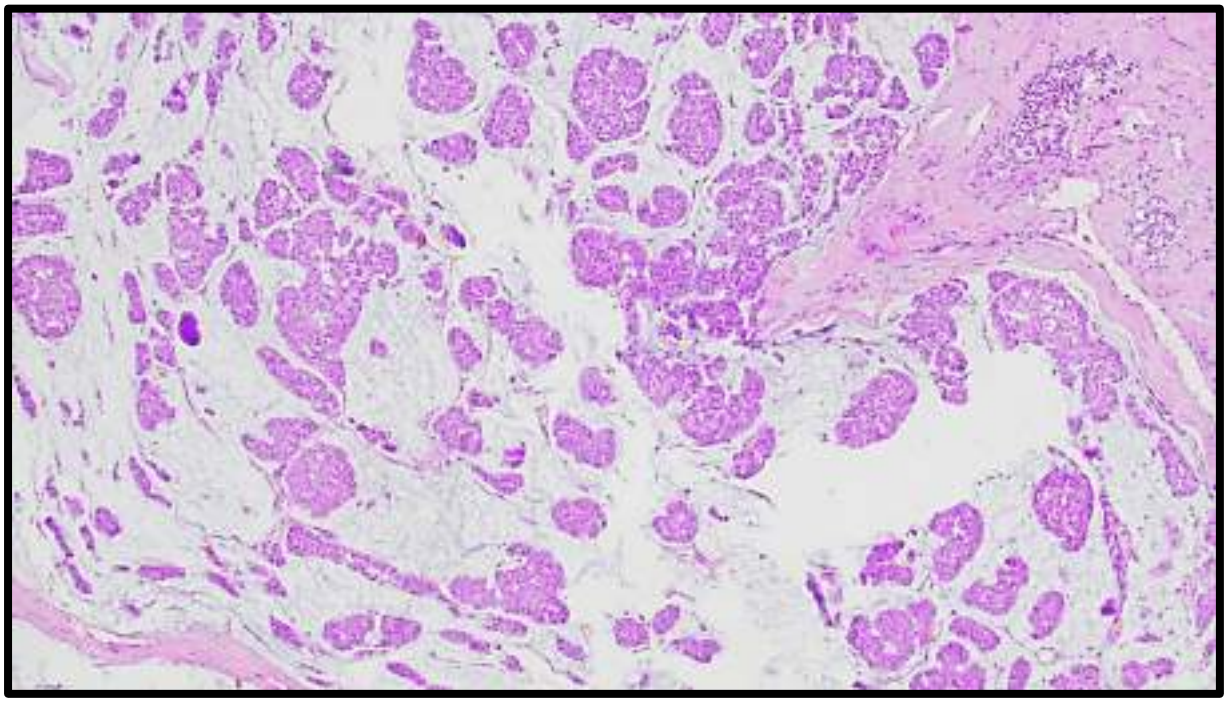
Picture 17- Photomicrograph showing periductular arrangement of tumor cells in Invasive Lobular Carcinoma (ILC) (H&E, 40X)



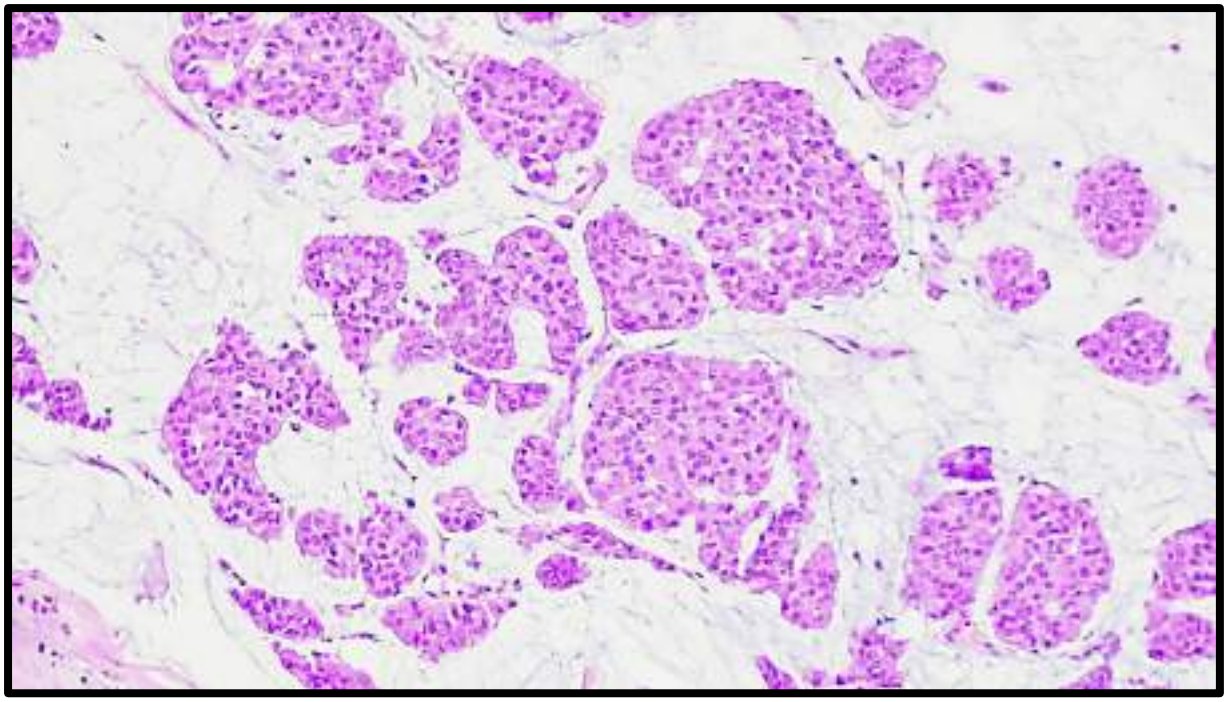
Picture 18- Photomicrograph showing Mixed IDC-NOS (blue arrow) and invasive lobular carcinoma (orange arrow) (H&E, 100X)



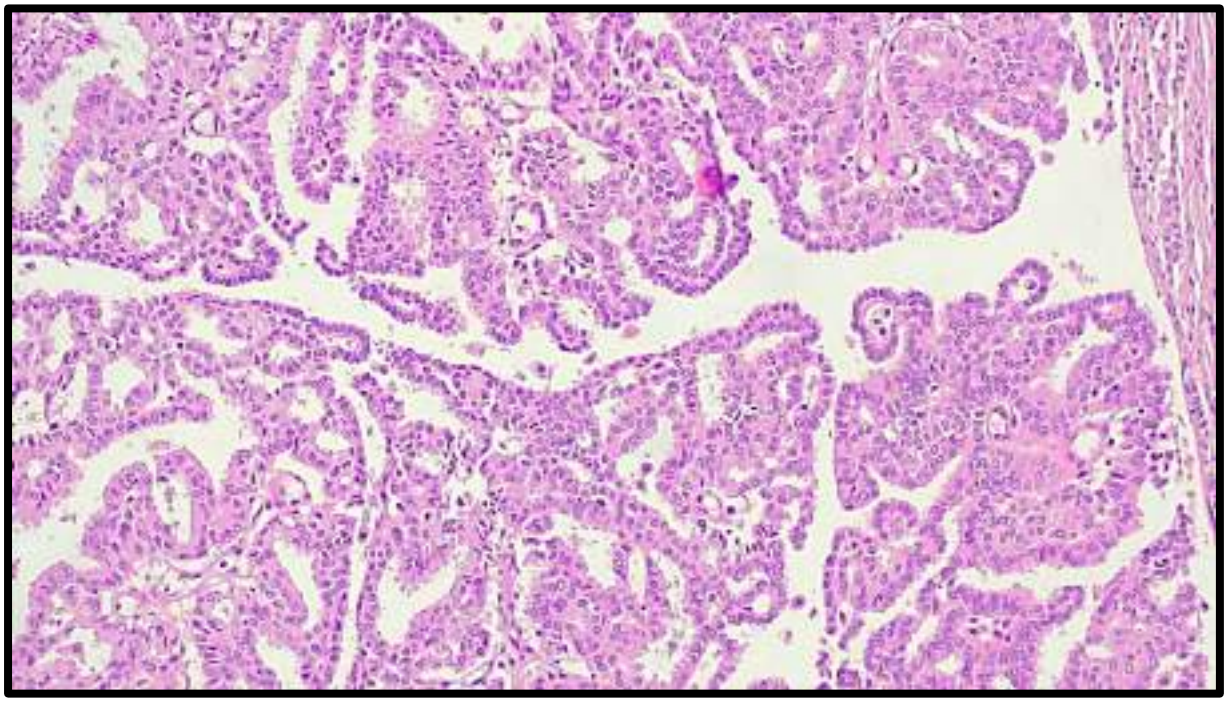
Picture 19- Photomicrograph of Infiltrating Duct Carcinoma with medullary pattern showing pushing borders and sheeting pattern. No tubule formation noted (H&E, 40X)



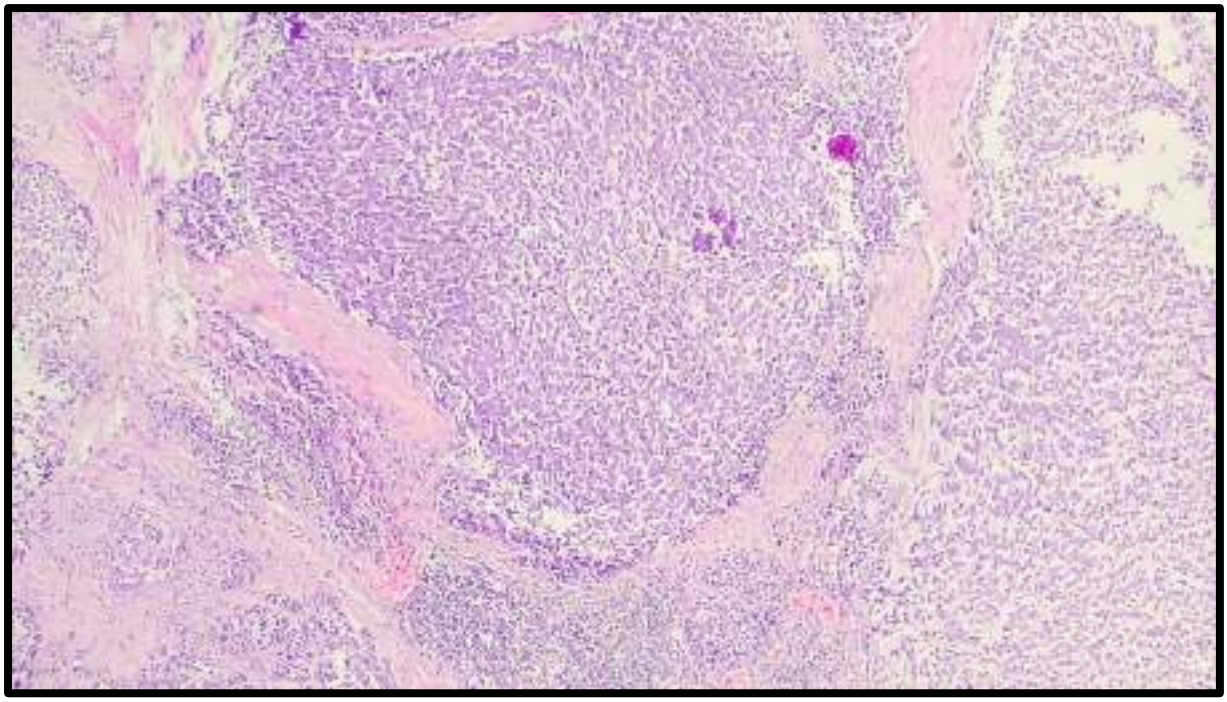
Picture 20- Photomicrograph of Mucinous carcinoma showing tumor cells floating in pools of extracellular mucin (H&E, 40X)



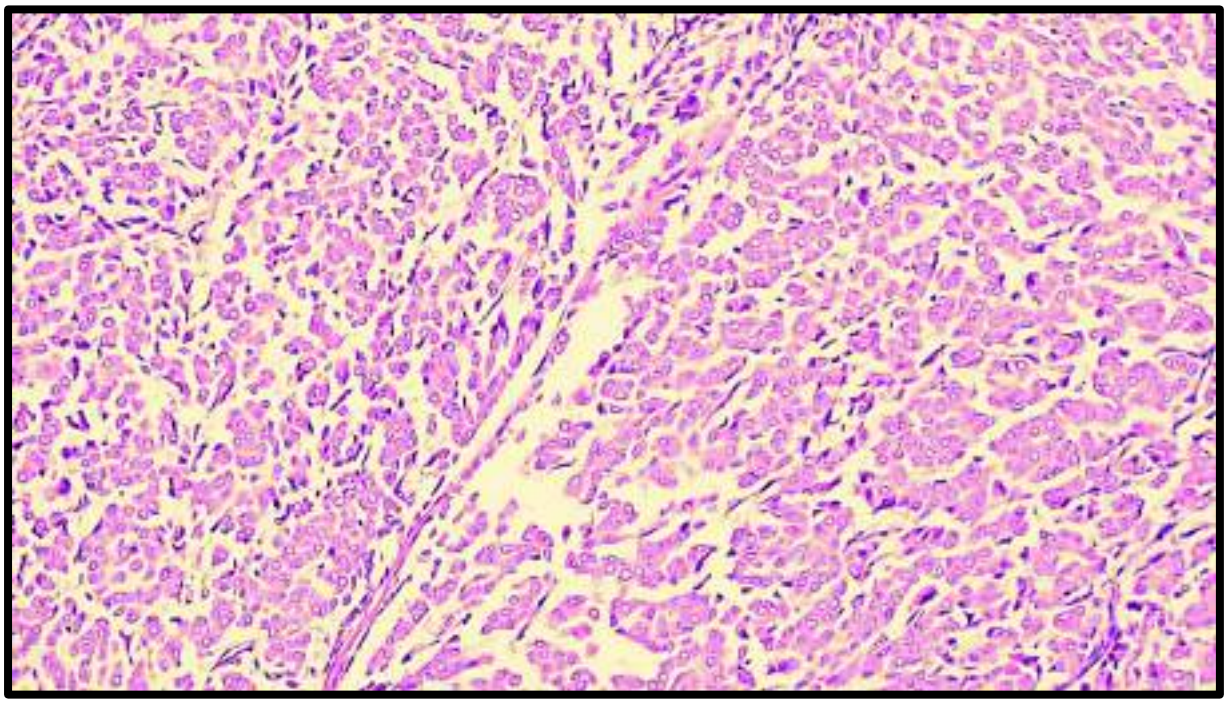
Picture 21- Photomicrograph of Mucinous carcinoma showing clusters of tumor cells present in pools of extracellular mucin (H&E, 100X)



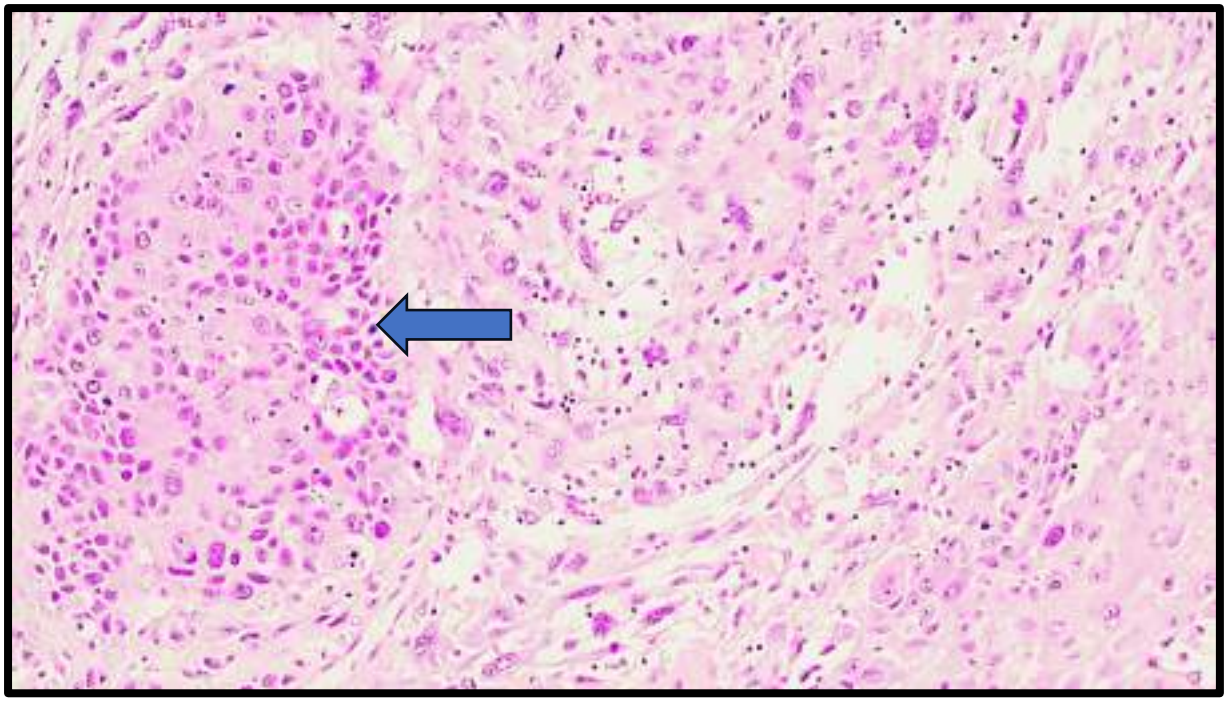
Picture 22- Photomicrograph of Papillary carcinoma showing true papillary growth pattern and absence of myoepithelial cells at the periphery and along the papillary stalks (H&E, 100X)



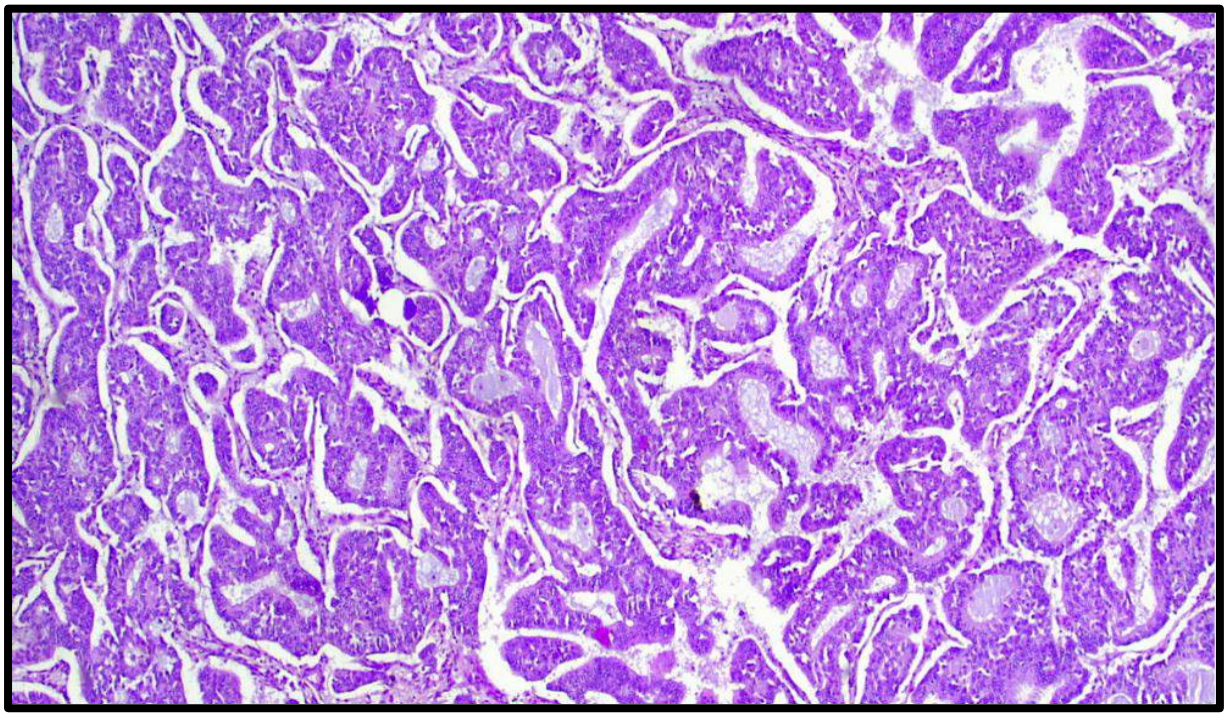
Picture 23- Photomicrograph of Solid papillary carcinoma showing nodules of tumor cells with a solid growth pattern (H&E, 40X)



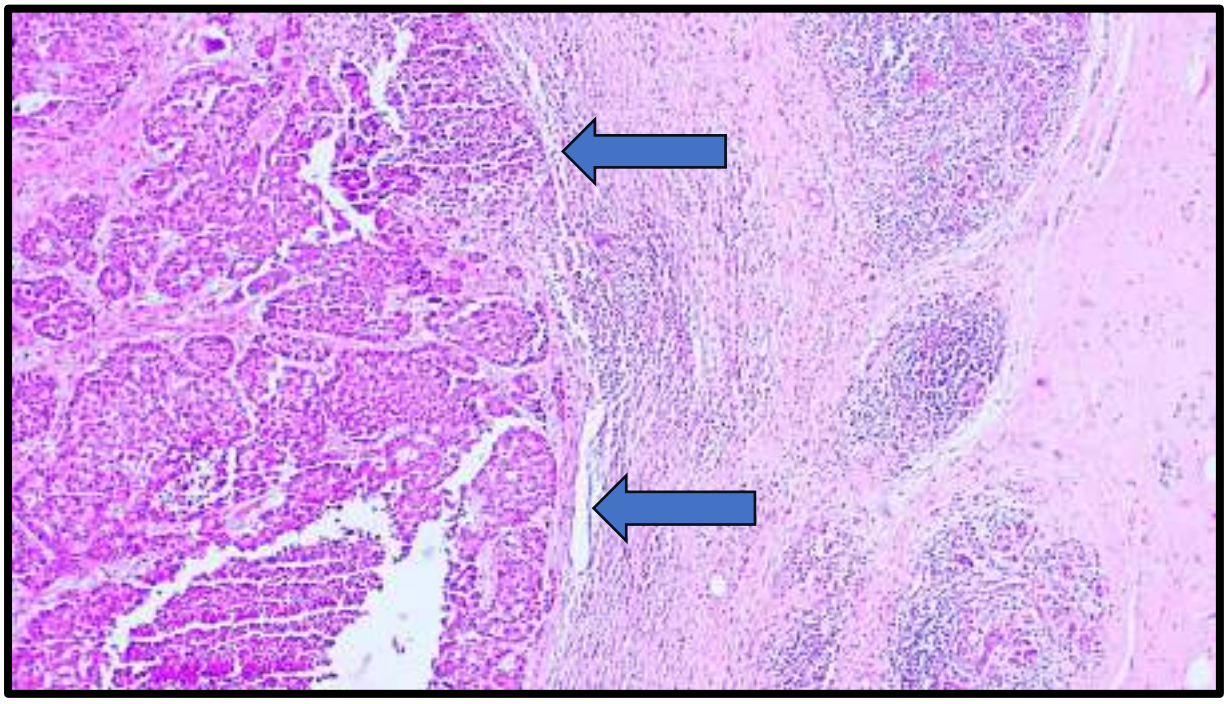
Picture 24- Photomicrograph of Solid papillary carcinoma with solid growth pattern and inconspicuous, delicate fibrovascular cores (H&E, 100X)



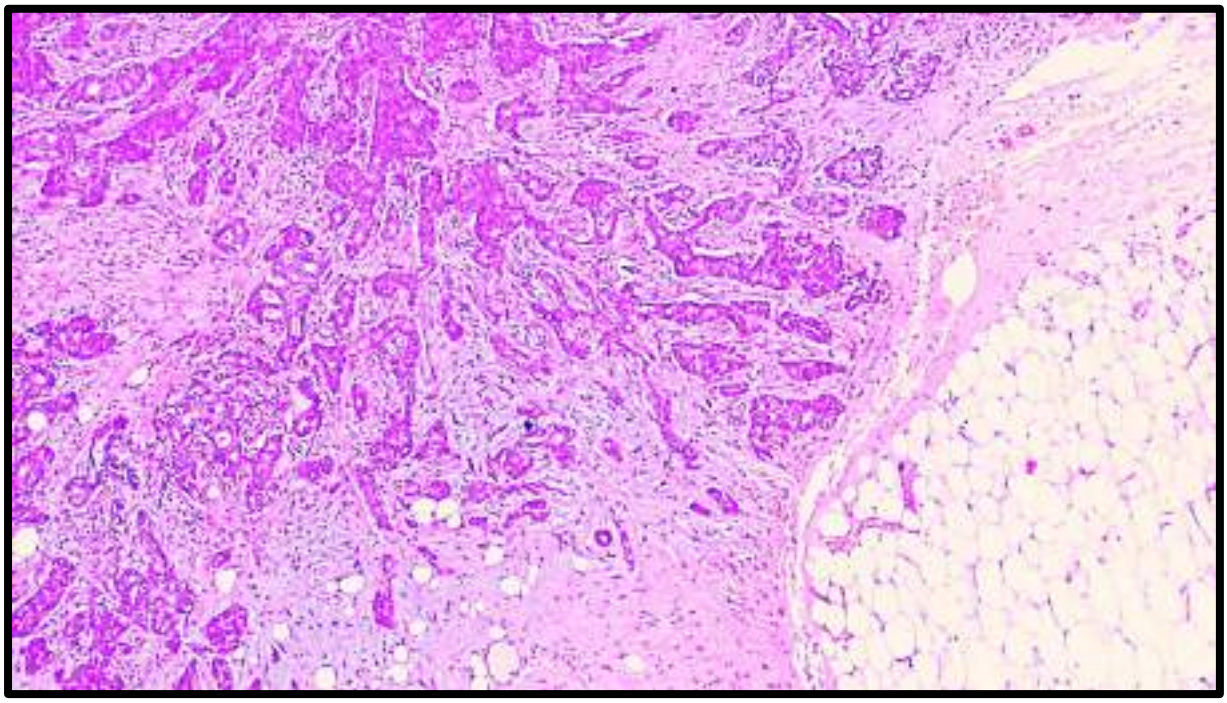
Picture 25- Photomicrograph of Metaplastic carcinoma showing showing presence of nests and clusters of tumor cells showing squamous differentiation (arrow) (H&E, 100X)



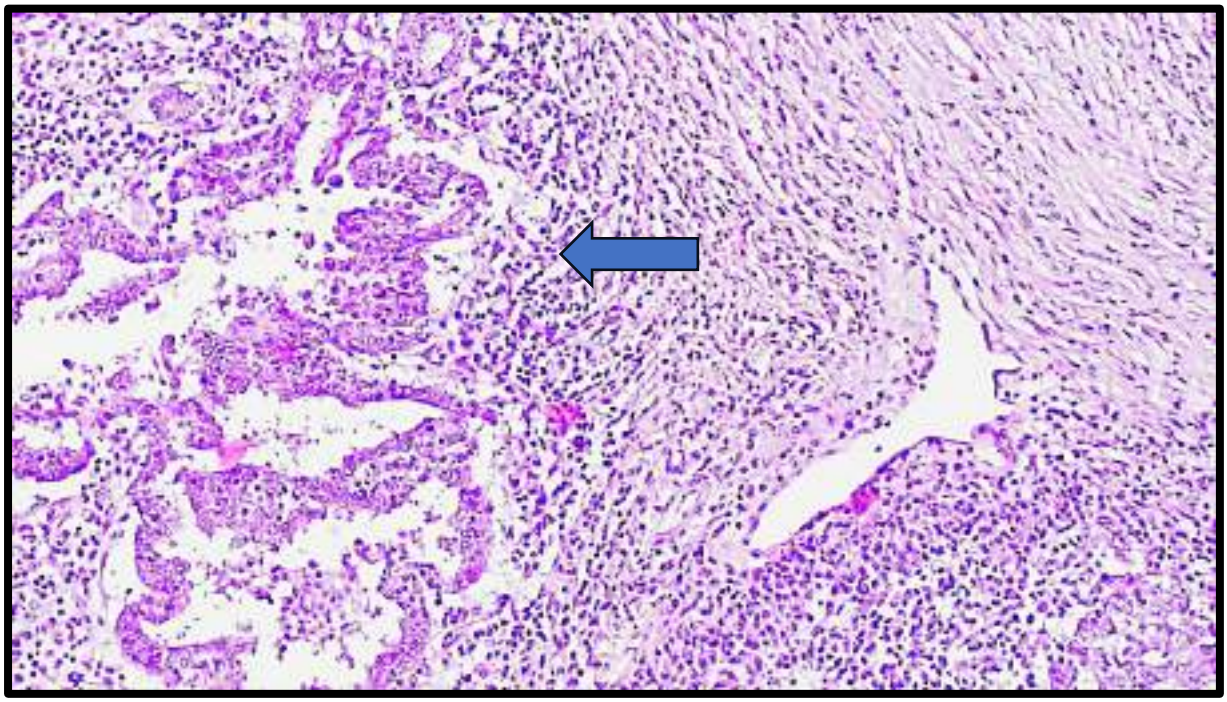
Picture 26- Photomicrograph of cribriform carcinoma showing well-defined cribriform spaces with tumor cells exhibiting mild nuclear atypia (H&E, 100X)



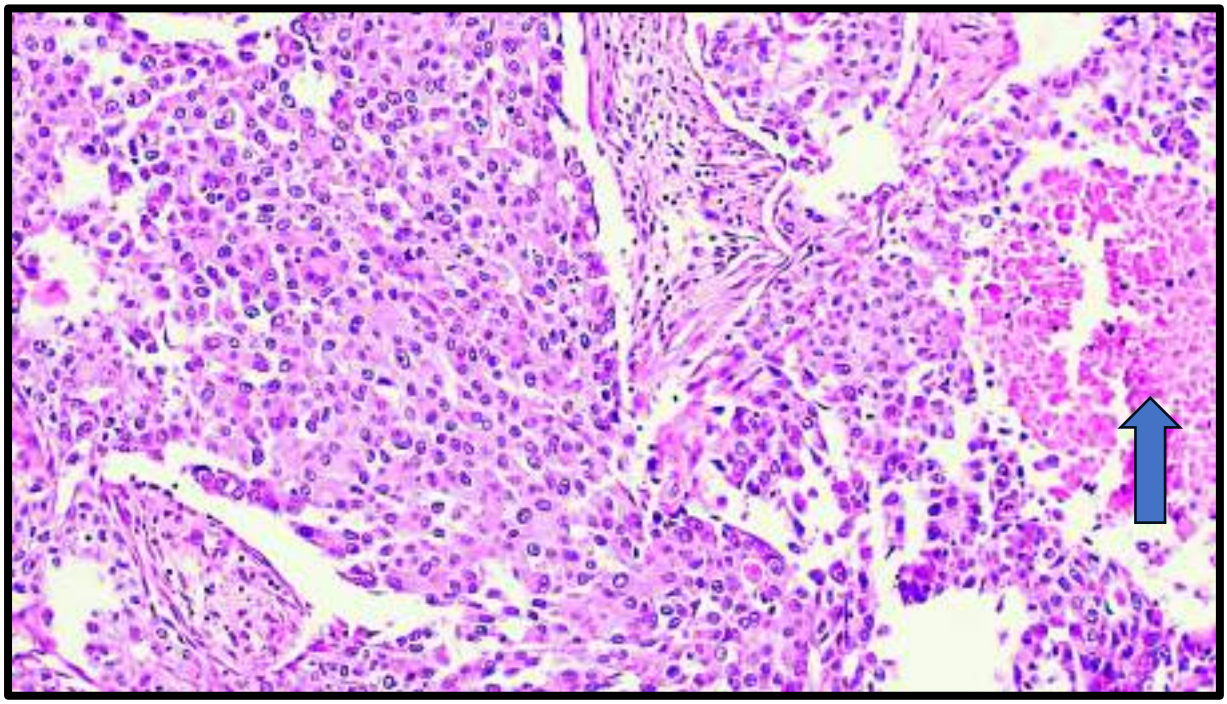
Picture 27- Photomicrograph showing pushing tumor margins (arrows) (H&E, 40X)



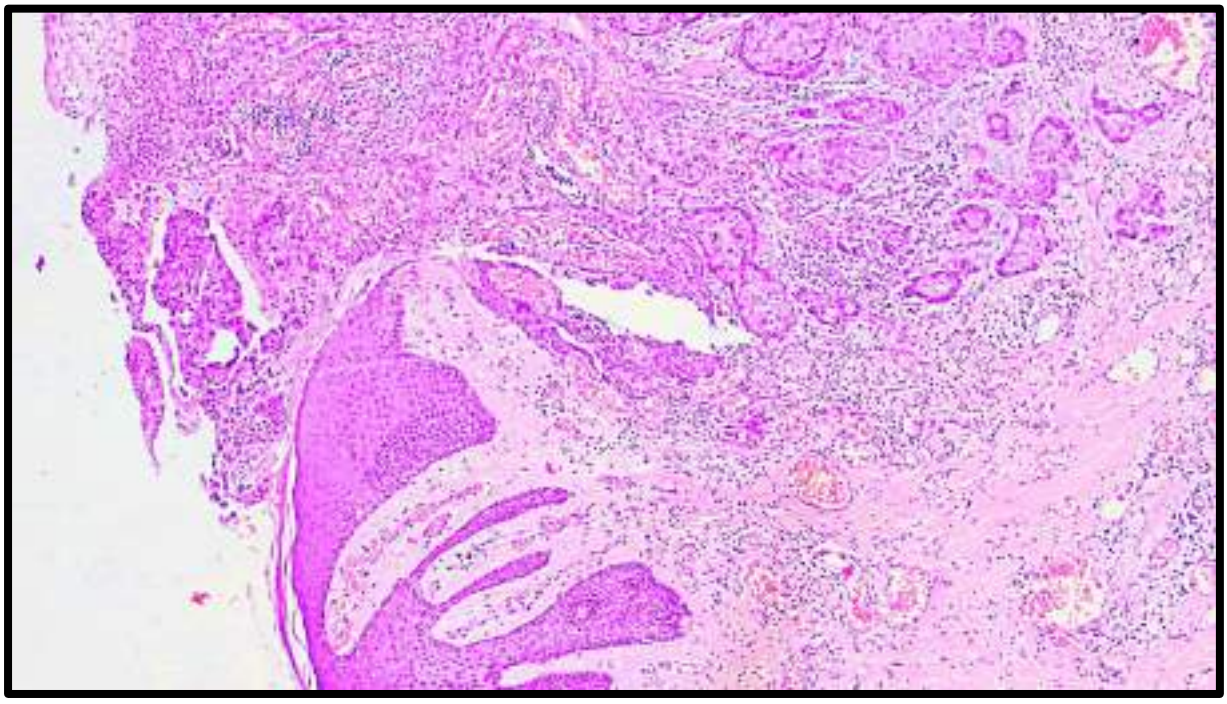
Picture 28- Photomicrograph showing infiltrating tumor margins (H&E, 40X)



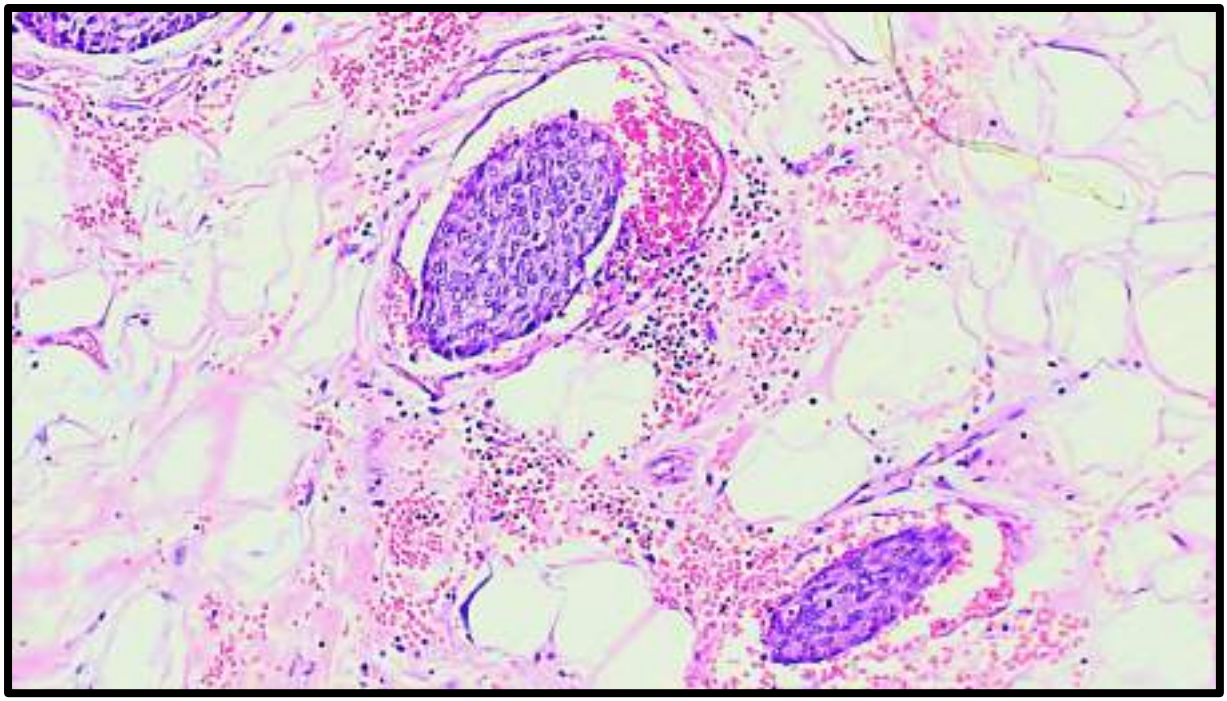
Picture 29- Photomicrograph showing marked lymphocytic response at the advancing tumor margins (arrows) (H&E, 100X)



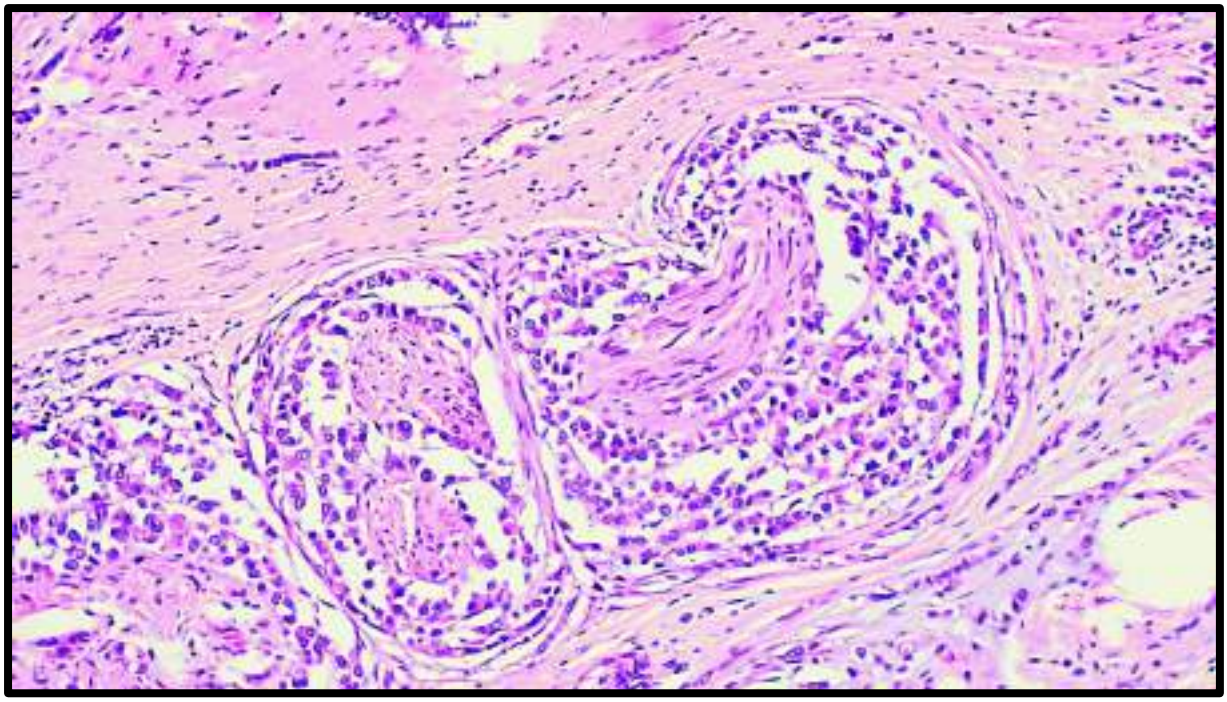
Picture 30- Photomicrograph showing tumor with presence of foci of necrosis (arrow) (H&E, 40X)



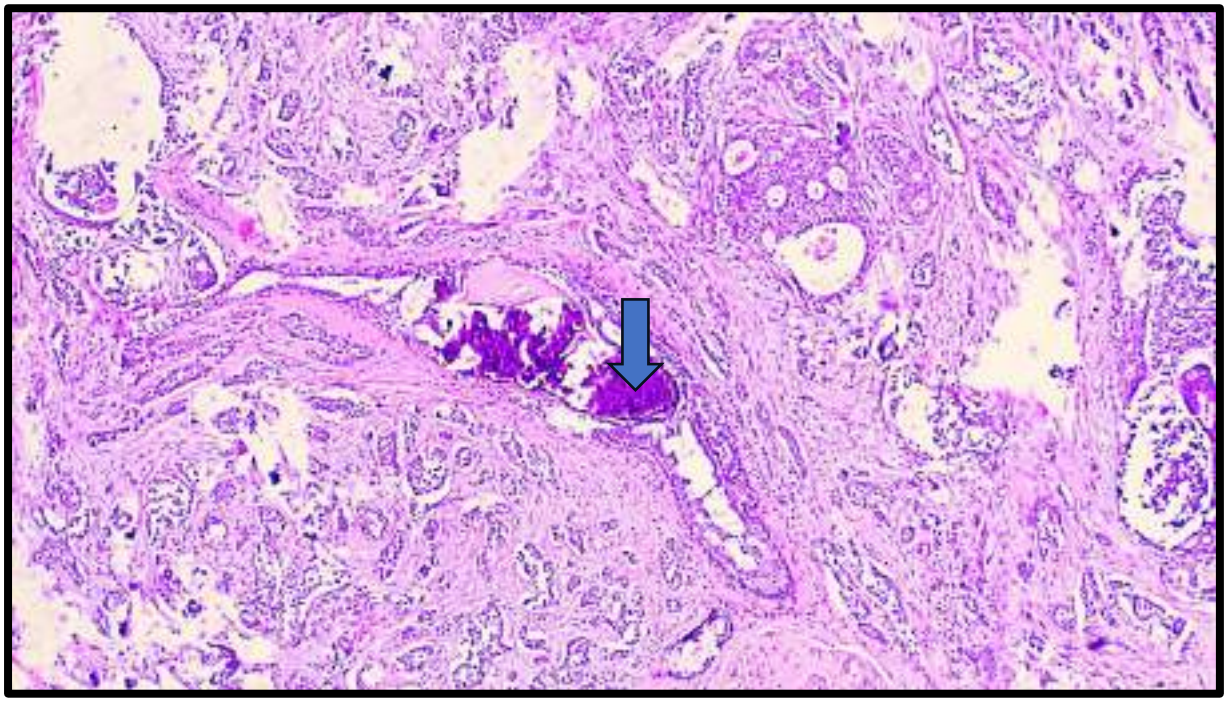
Picture 31- Photomicrograph showing tumor cells causing skin ulceration (H&E, 100X)



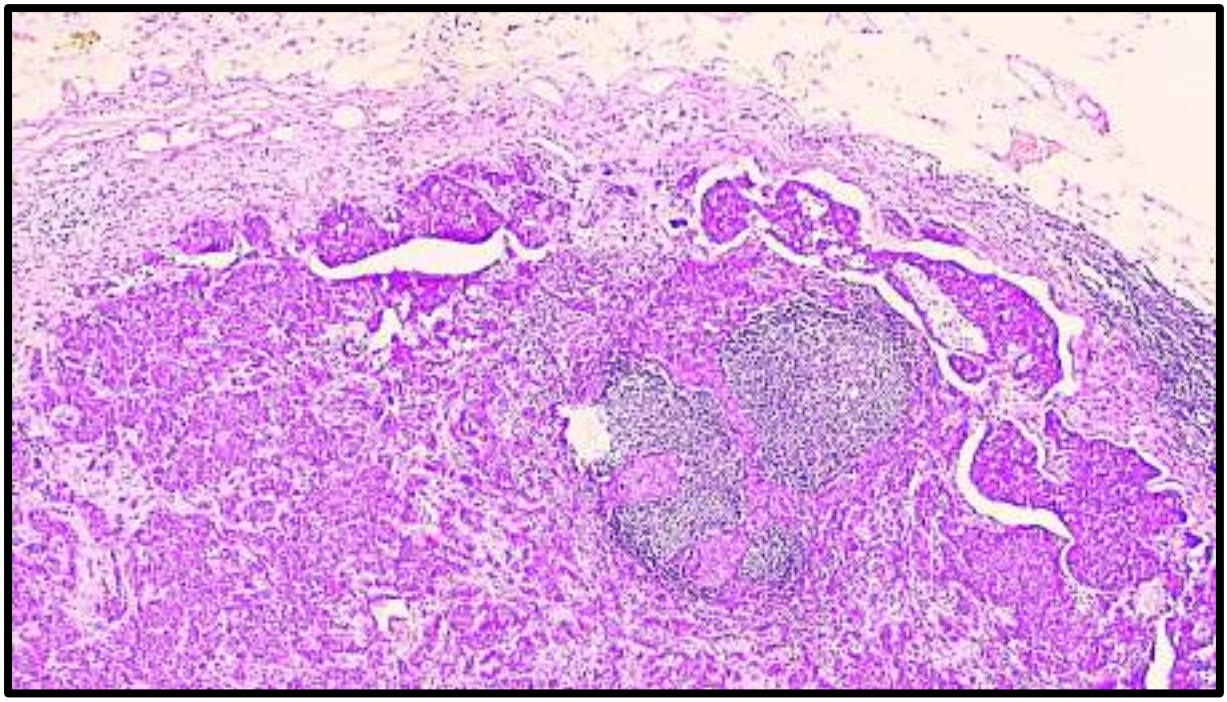
Picture 32- Photomicrograph showing lymphovascular invasion (LVI) (H&E, 100X)



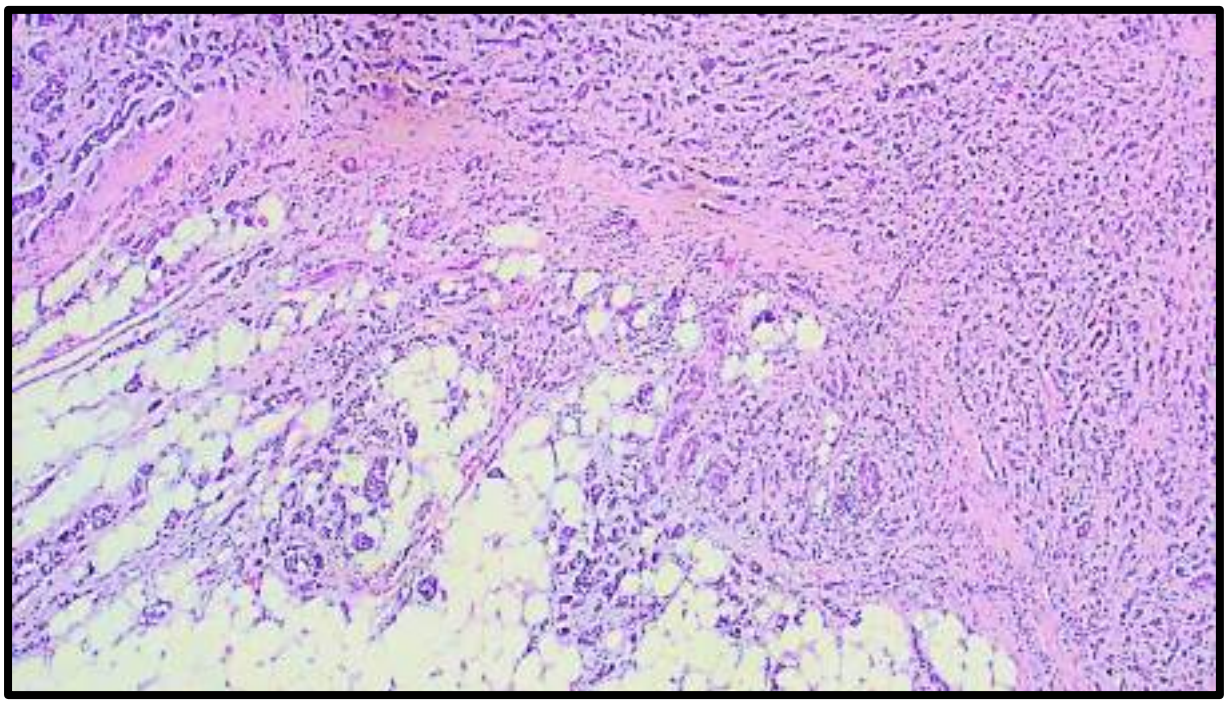
Picture 33- Photomicrograph showing perineural invasion (H&E, 100X)



Picture 34- Photomicrograph of tumor showing microcalcifications (arrow) (H&E, 40X)



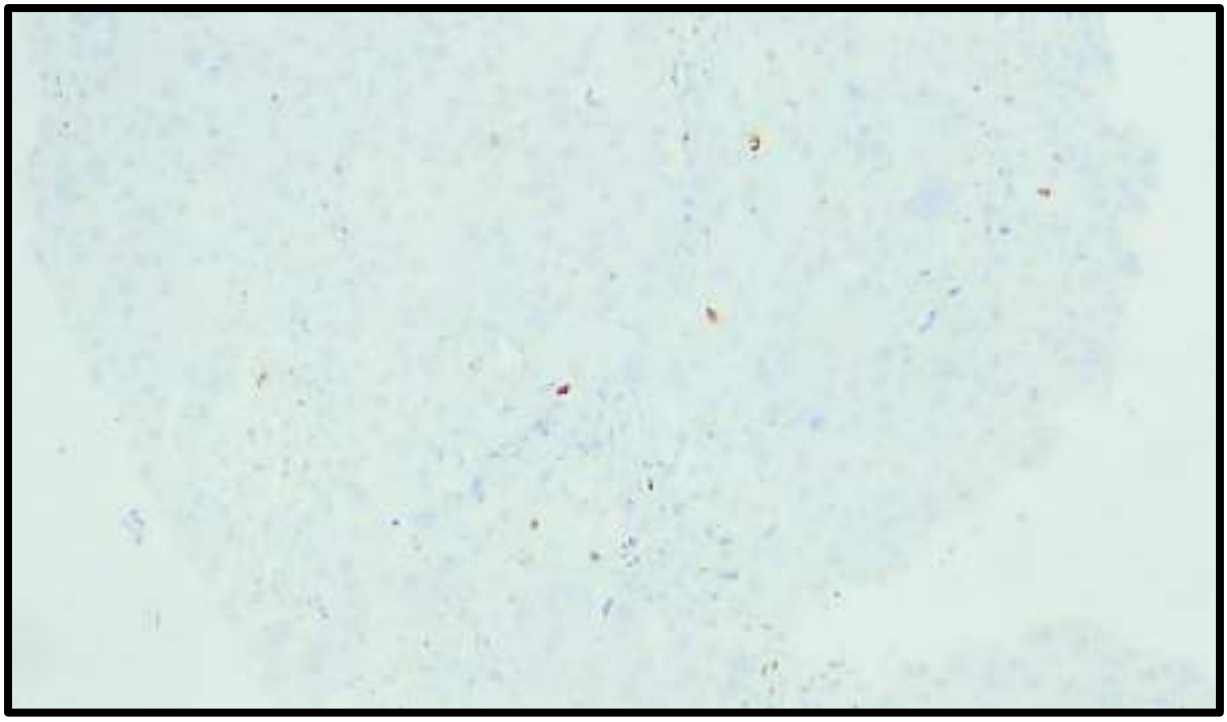
Picture 35- Photomicrograph showing metastatic carcinomatous deposits- lymph node (H&E,100X)



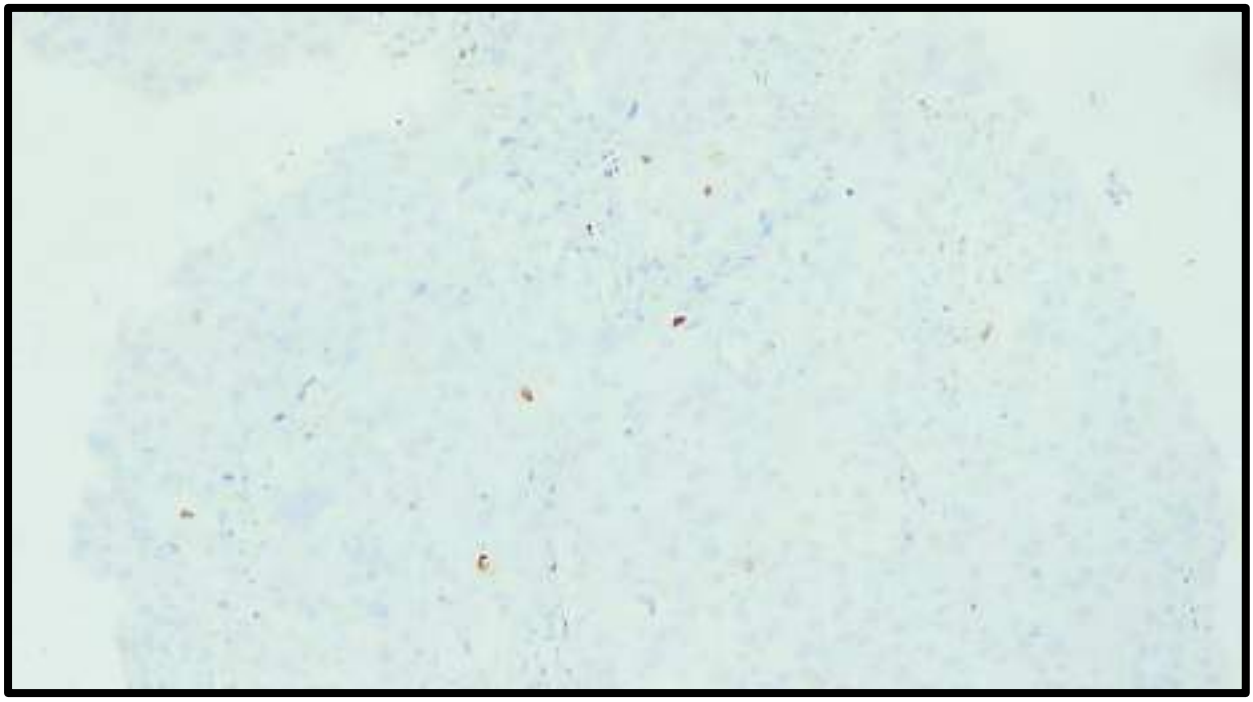
Picture 36- Photomicrograph showing extranodal extension with area of tumor invasion outside the lymph node capsule (H&E, 40X)

Picture 37- Photomicrograph of Estrogen Receptor (ER) = 0/8 (Proportional Score+Intensity Score) (IHC, 100X)

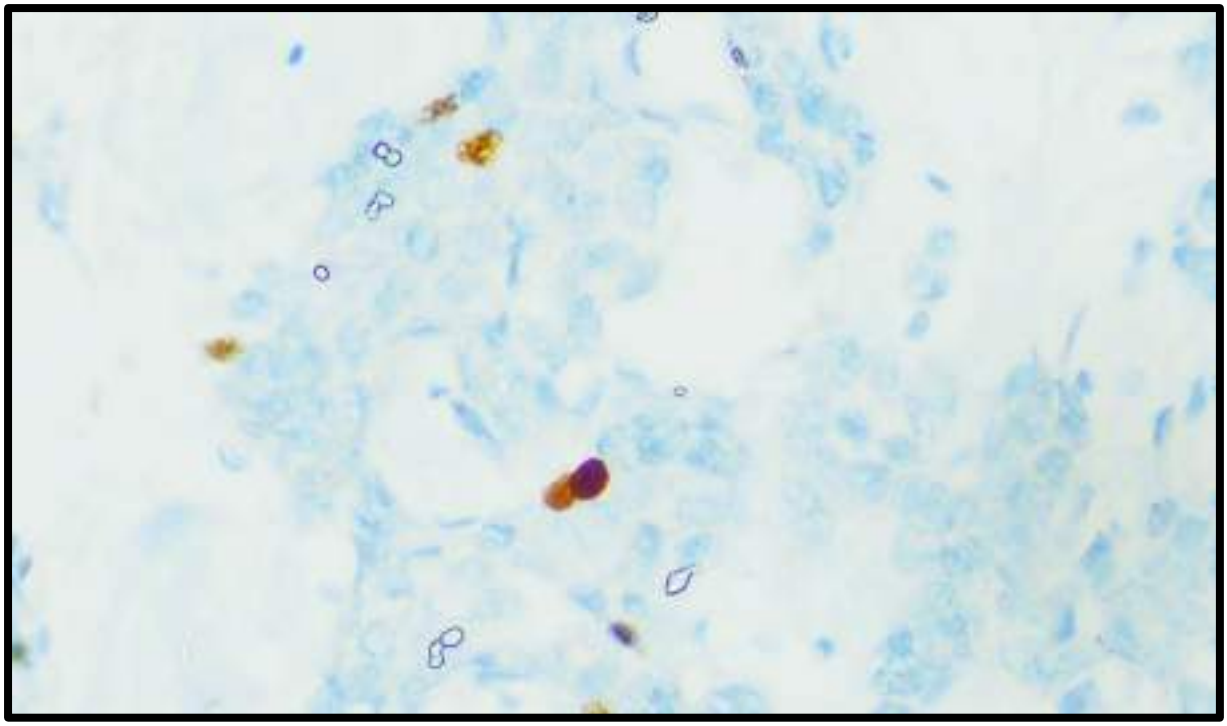
Picture 38- Photomicrograph of Progesterone Receptor (PR)= 0/8 (Proportional Score+Intensity Score) (IHC, 100X)



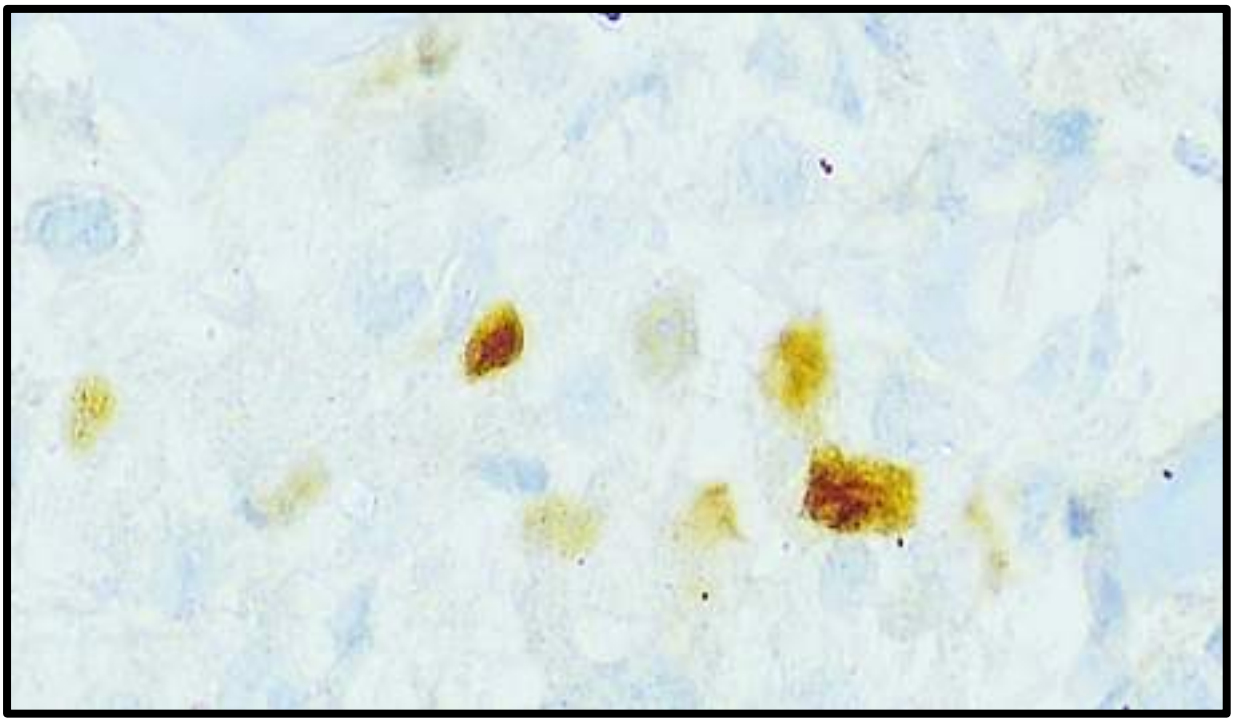
Picture 39- Photomicrograph of Estrogen Receptor (ER) interpretation = 2/8 (Proportional Score+Intensity Score) (IHC, 100X)



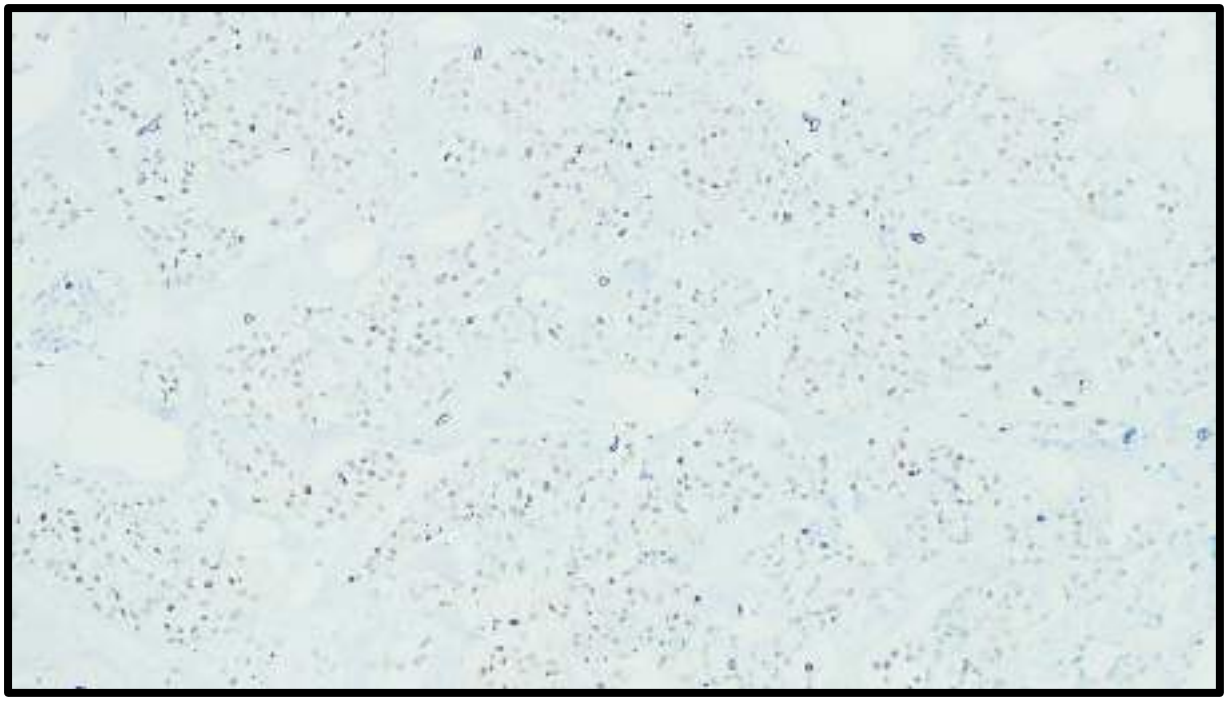
Picture 40- Photomicrograph of Progesterone Receptor (PR) interpretation = 2/8 (Proportional Score+Intensity Score) (IHC, 100X)



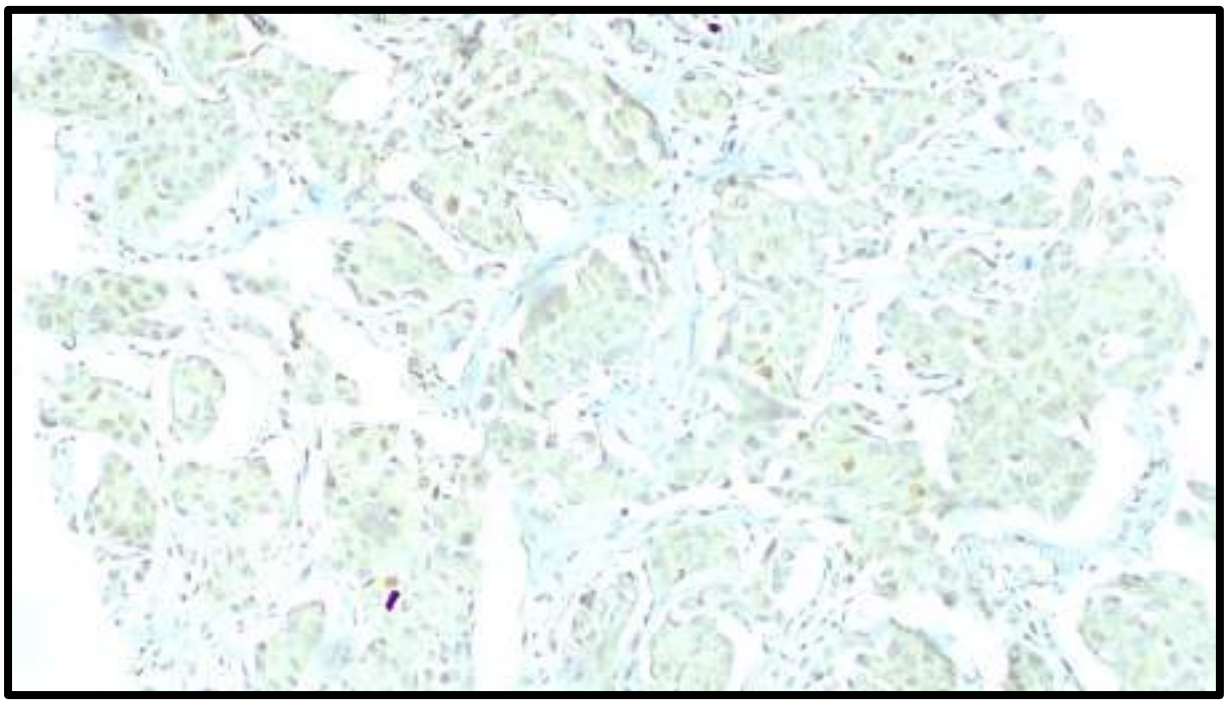
Picture 41- Photomicrograph of Estrogen Receptor (ER) interpretation = 3/8 (Proportional Score+Intensity Score) (IHC, 400X)



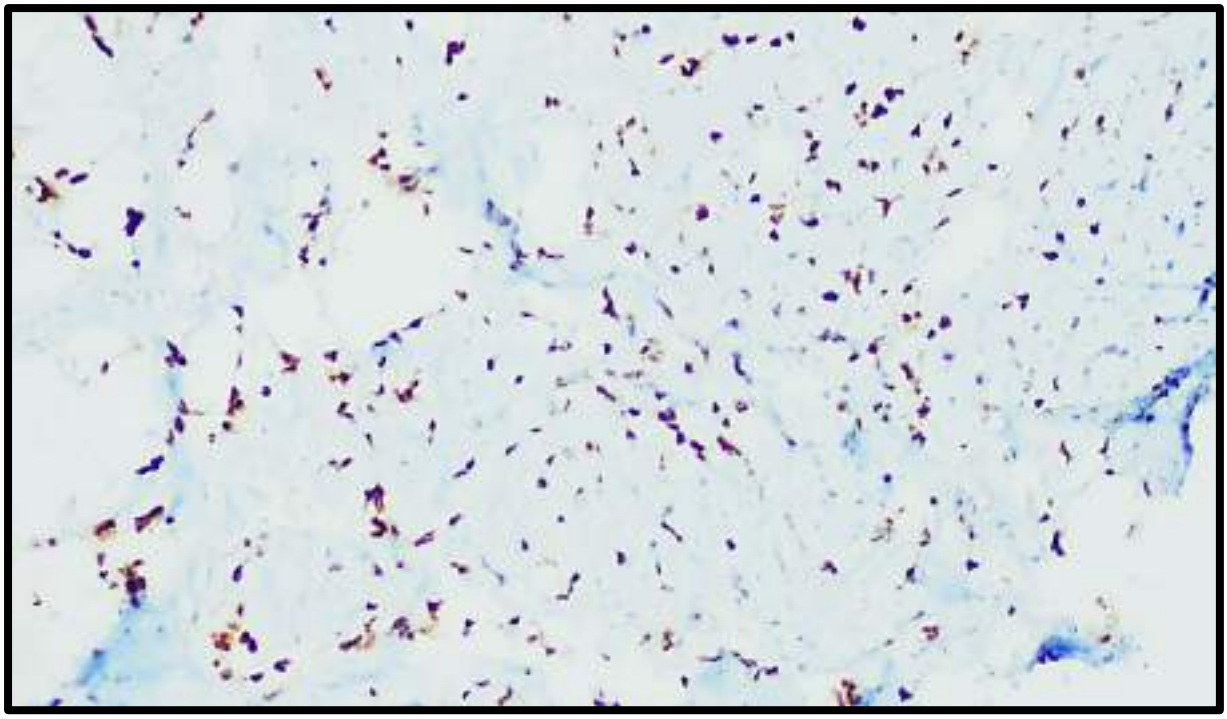
Picture 42- Photomicrograph of Progesterone Receptor (PR) interpretation = 3/8 (Proportional Score+Intensity Score) (IHC, 400X)



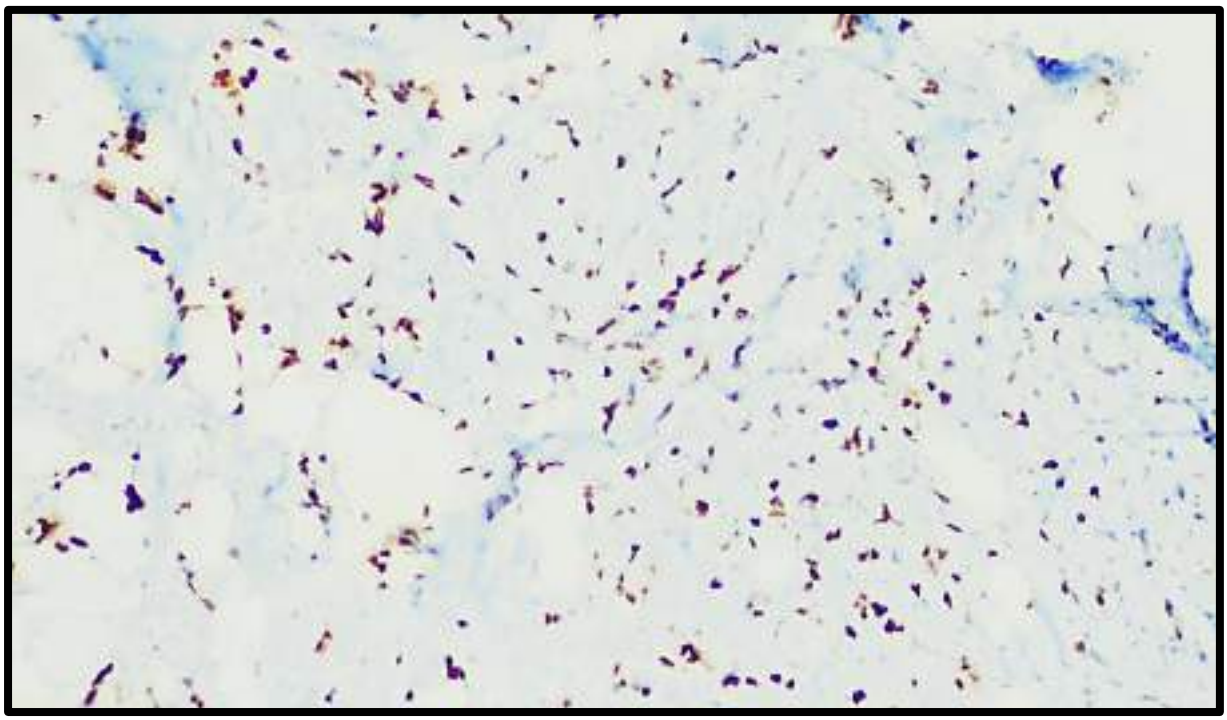
Picture 43- Photomicrograph of Estrogen Receptor (ER) interpretation = 4/8 (Proportional Score+Intensity Score) (IHC, 40X)



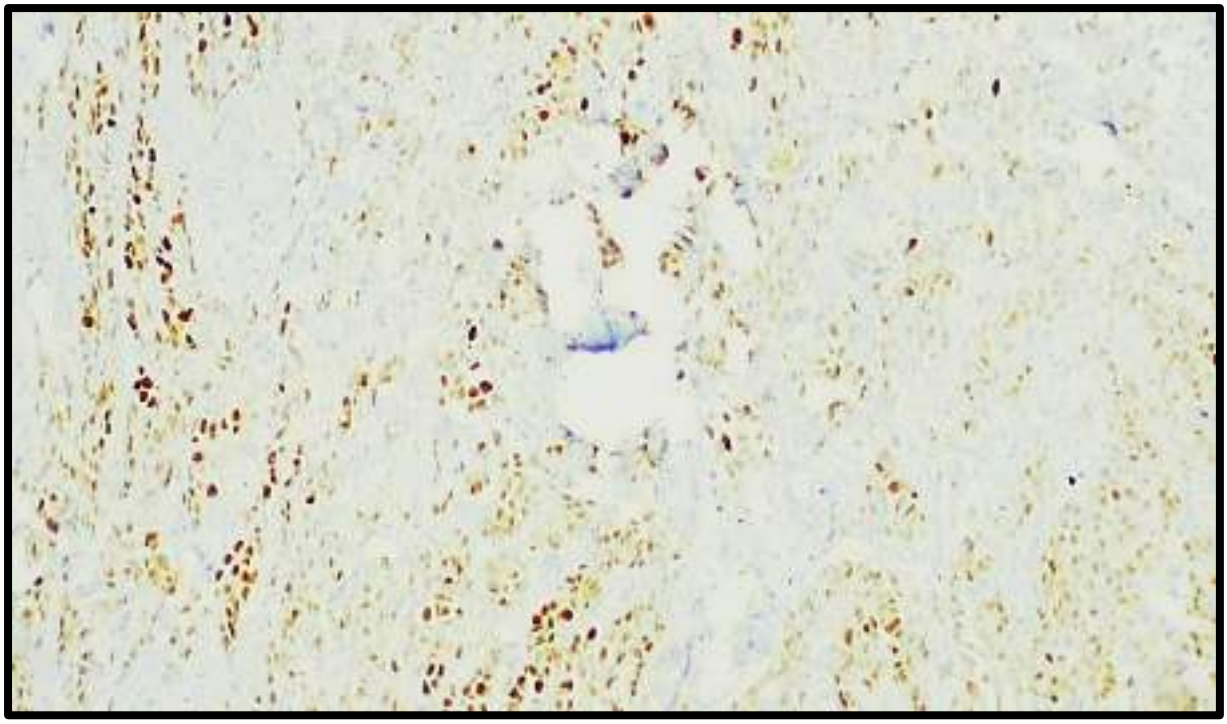
Picture 44- Photomicrograph of Progesterone Receptor (PR) interpretation = 4/8 (Proportional Score+Intensity Score) (IHC, 100X)



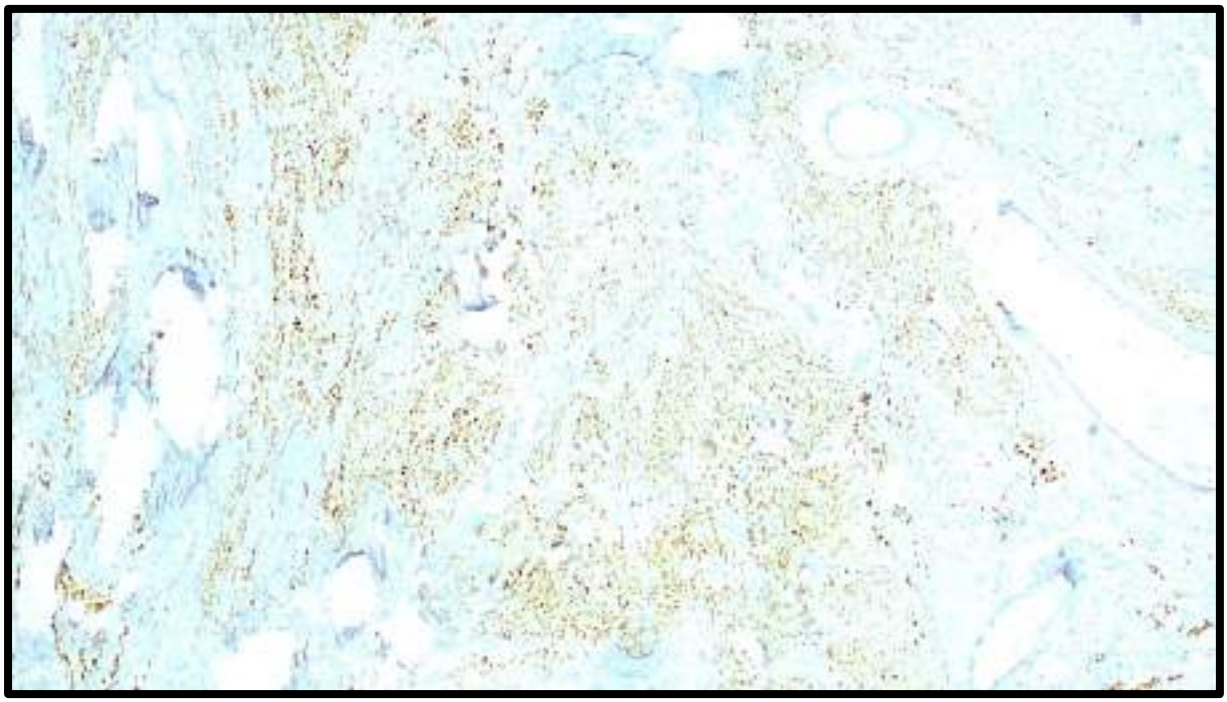
Picture 45- Photomicrograph of Estrogen Receptor (ER) interpretation = 5/8 (Proportional Score+Intensity Score) (IHC, 100X)



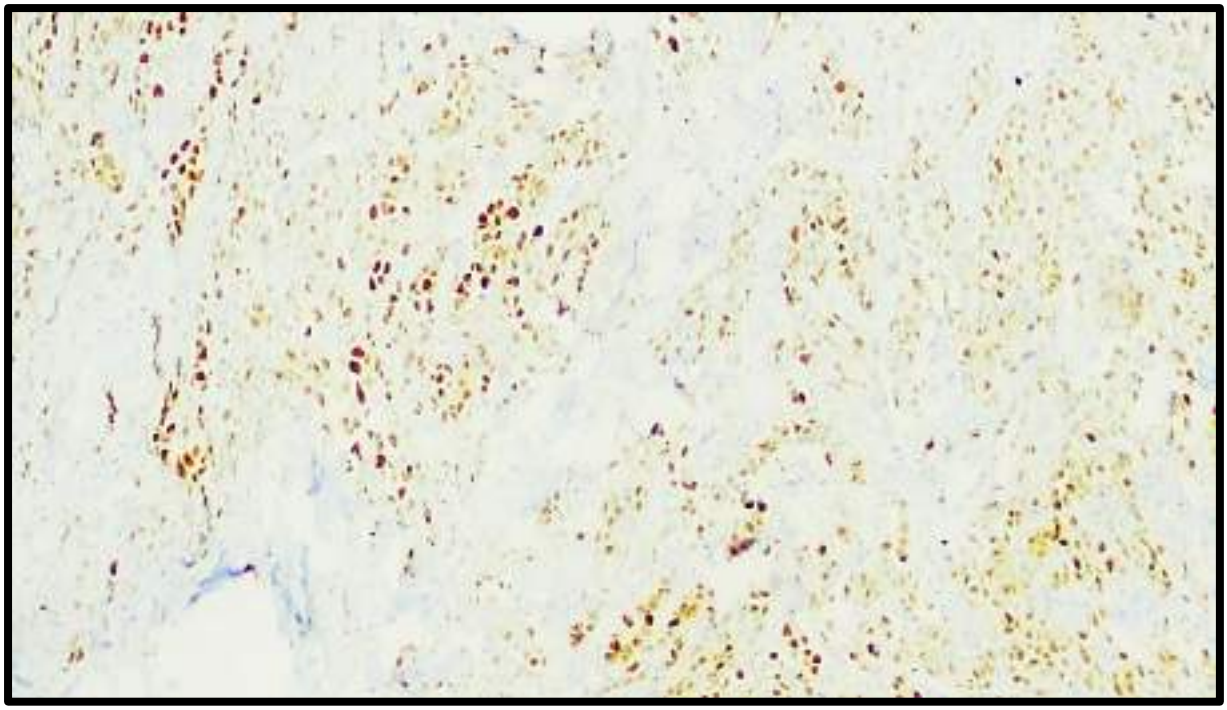
Picture 46- Photomicrograph of Progesterone Receptor (PR) interpretation = 5/8 (Proportional Score+Intensity Score) (IHC, 100X)



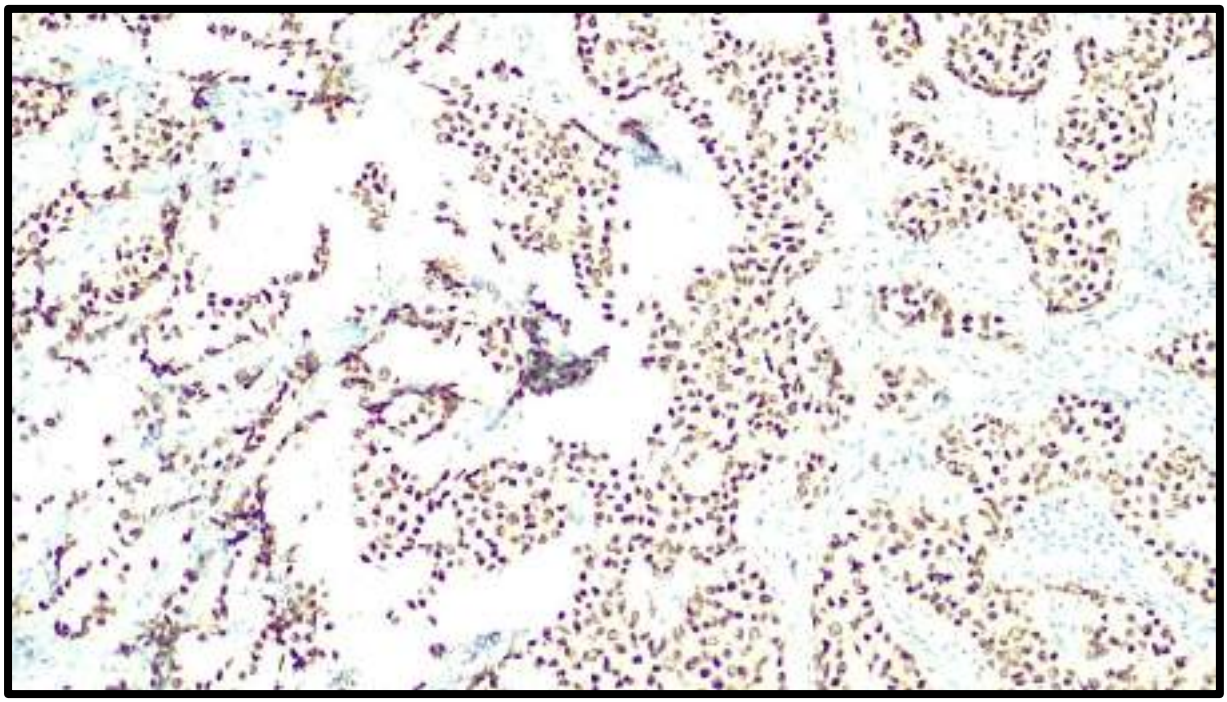
Picture 47- Photomicrograph of Estrogen Receptor (ER) interpretation = 6/8 (Proportional Score+Intensity Score) (IHC, 40X)



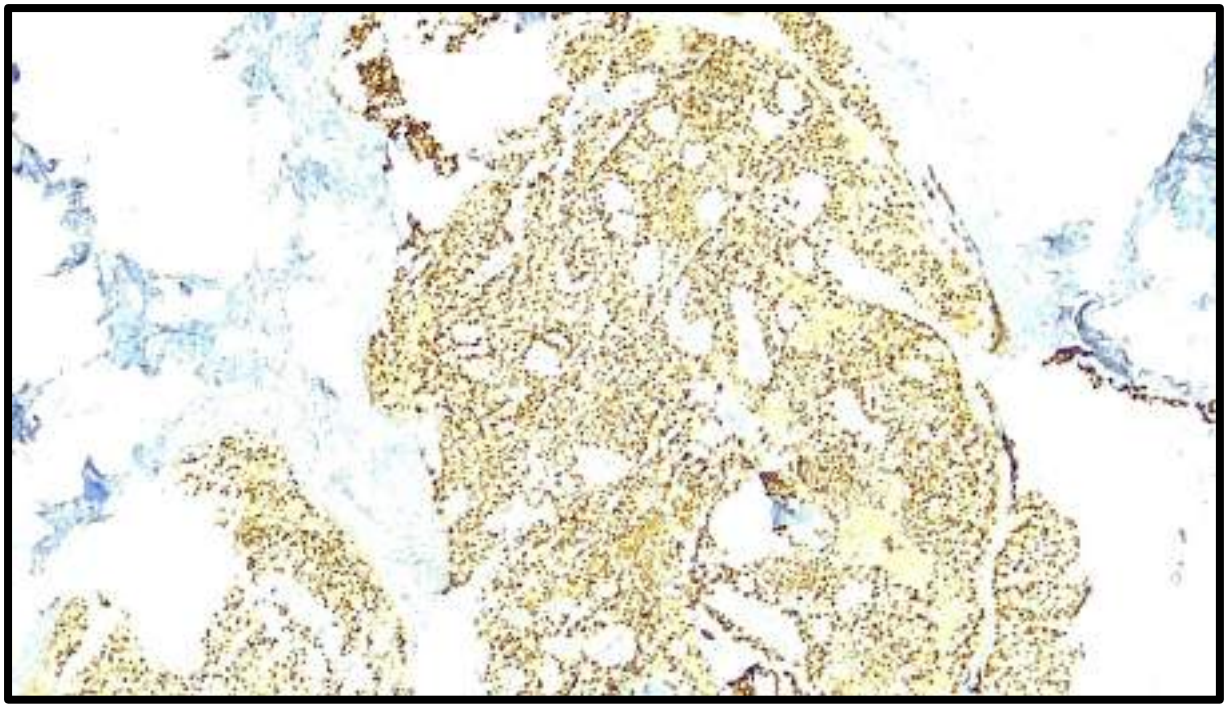
Picture 48- Photomicrograph of Progesterone Receptor (PR) interpretation = 6/8 (Proportional Score+Intensity Score) (IHC, 40X)



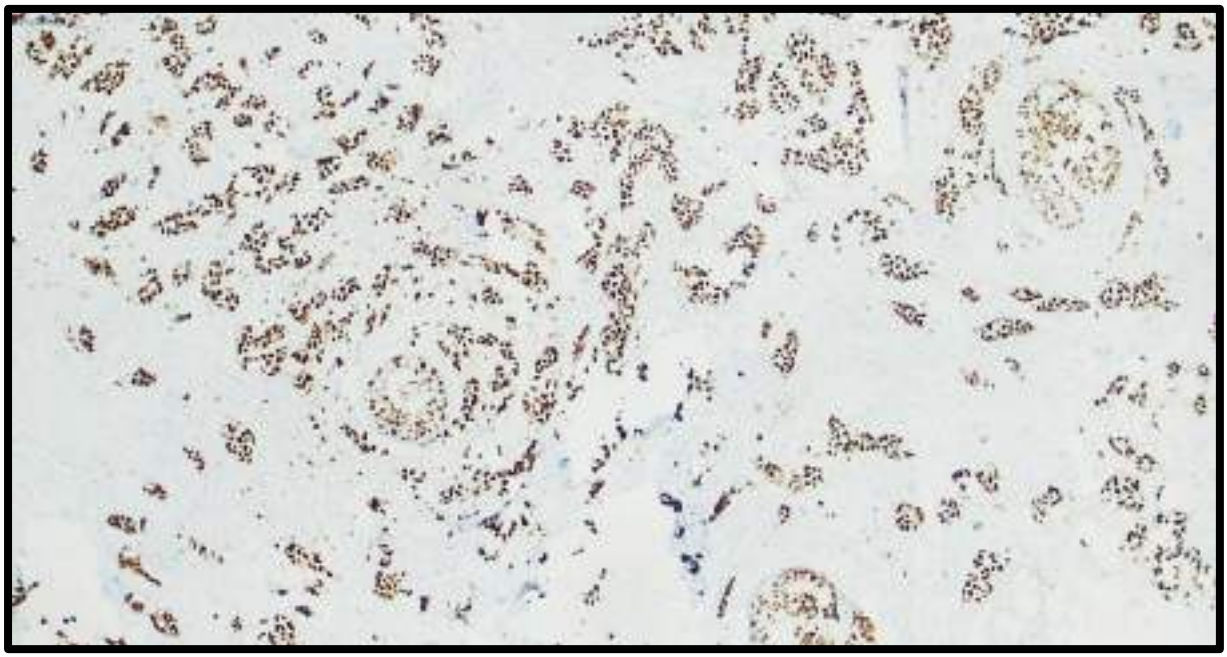
Picture 49- Photomicrograph of Estrogen Receptor (ER) interpretation = 7/8 (Proportional Score+Intensity Score) (IHC, 40X)



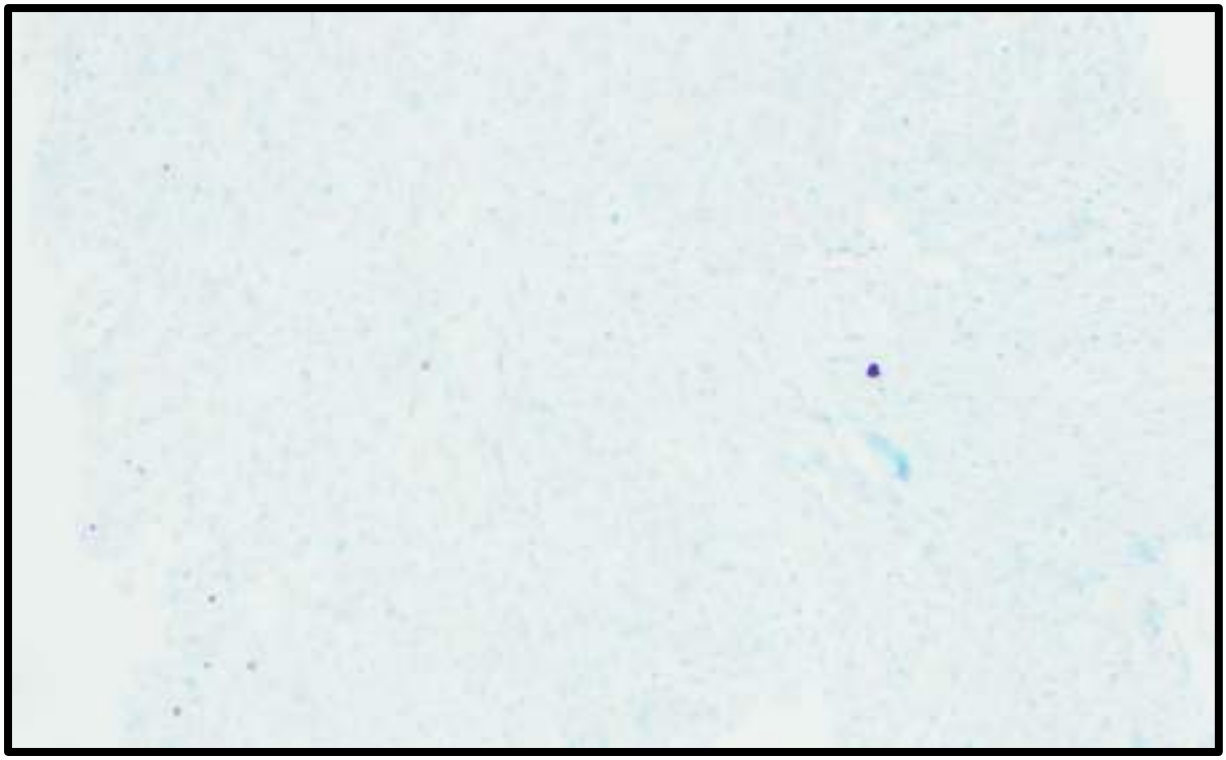
Picture 50- Photomicrograph of Progesterone Receptor (PR) interpretation = 7/8 (Proportional Score+Intensity Score) (IHC, 40X)



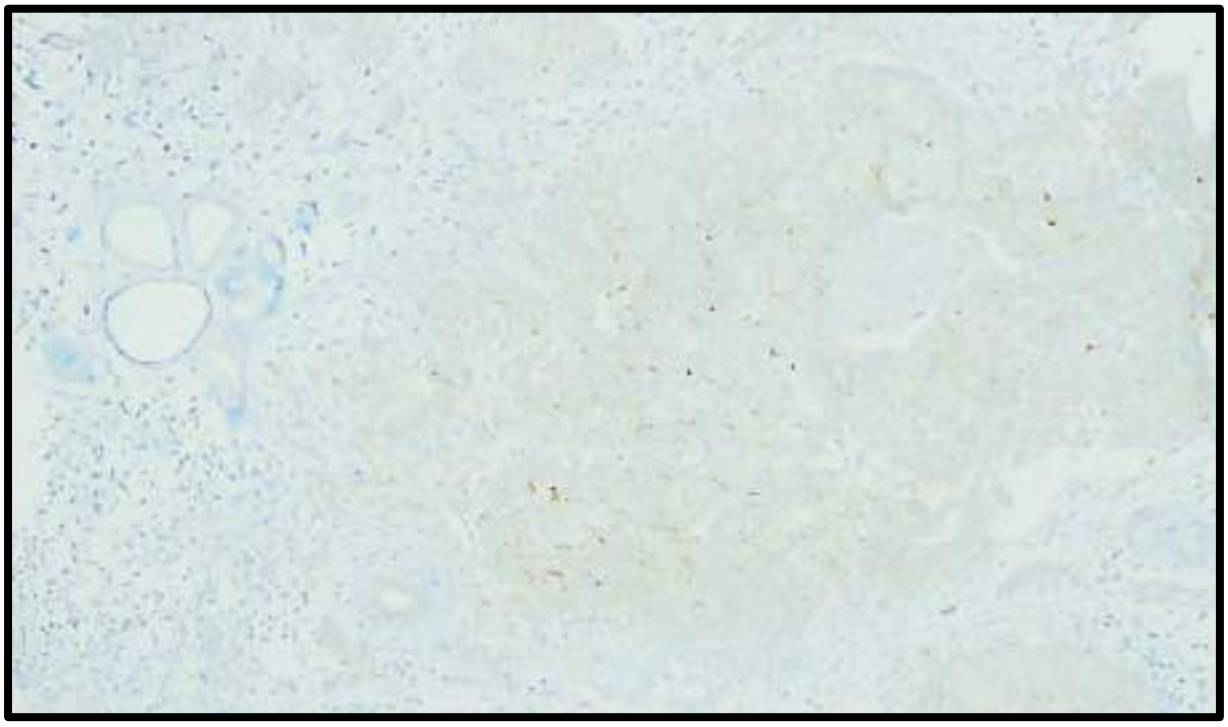
Picture 51- Photomicrograph of Estrogen Receptor (ER) interpretation = 8/8 (Proportional Score+Intensity Score) (IHC, 40X)



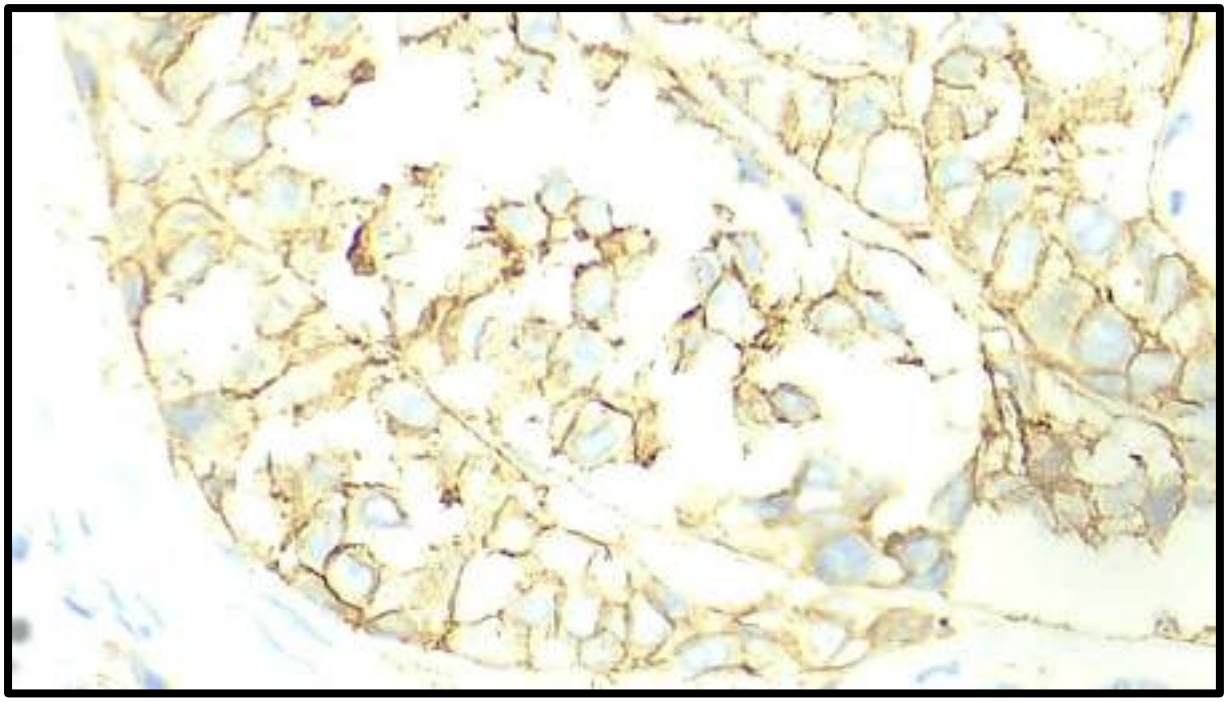
Picture 52- Photomicrograph of Progesterone Receptor (PR) interpretation = 8/8 (Proportional Score+Intensity Score) (IHC, 40X)



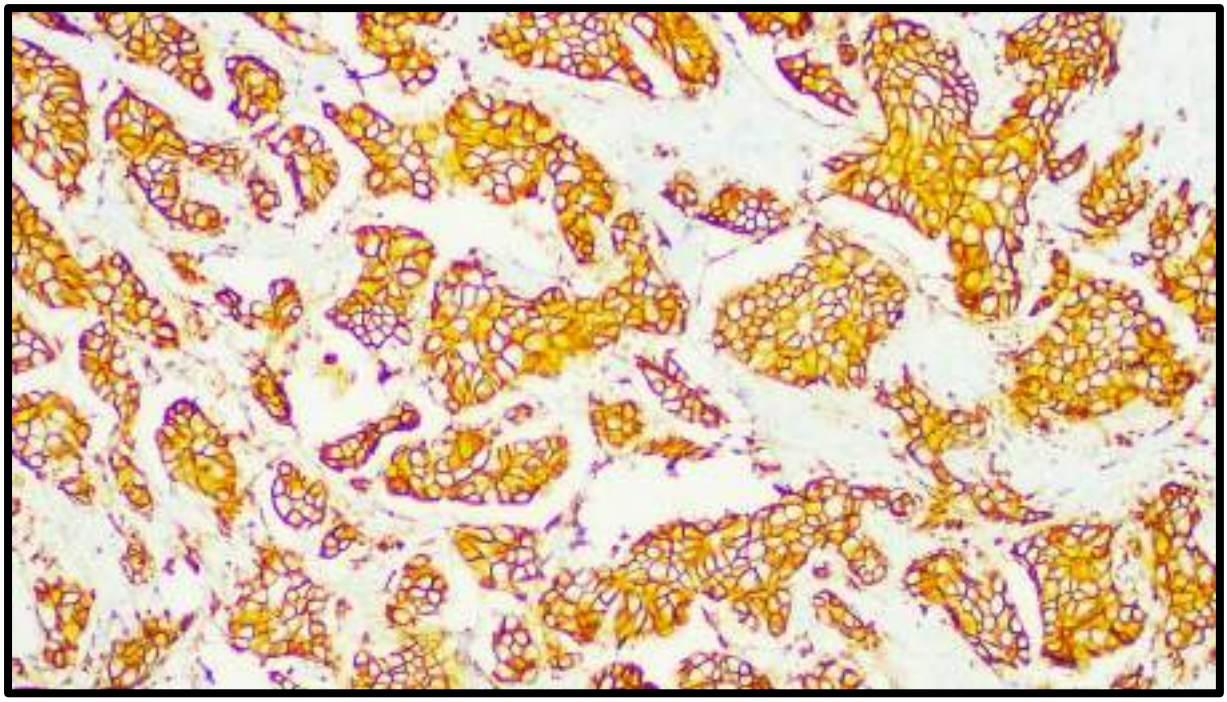
Picture 53- Photomicrograph of HER 2/ neu interpretation = 0 (Negative), showing no staining (IHC, 100X)



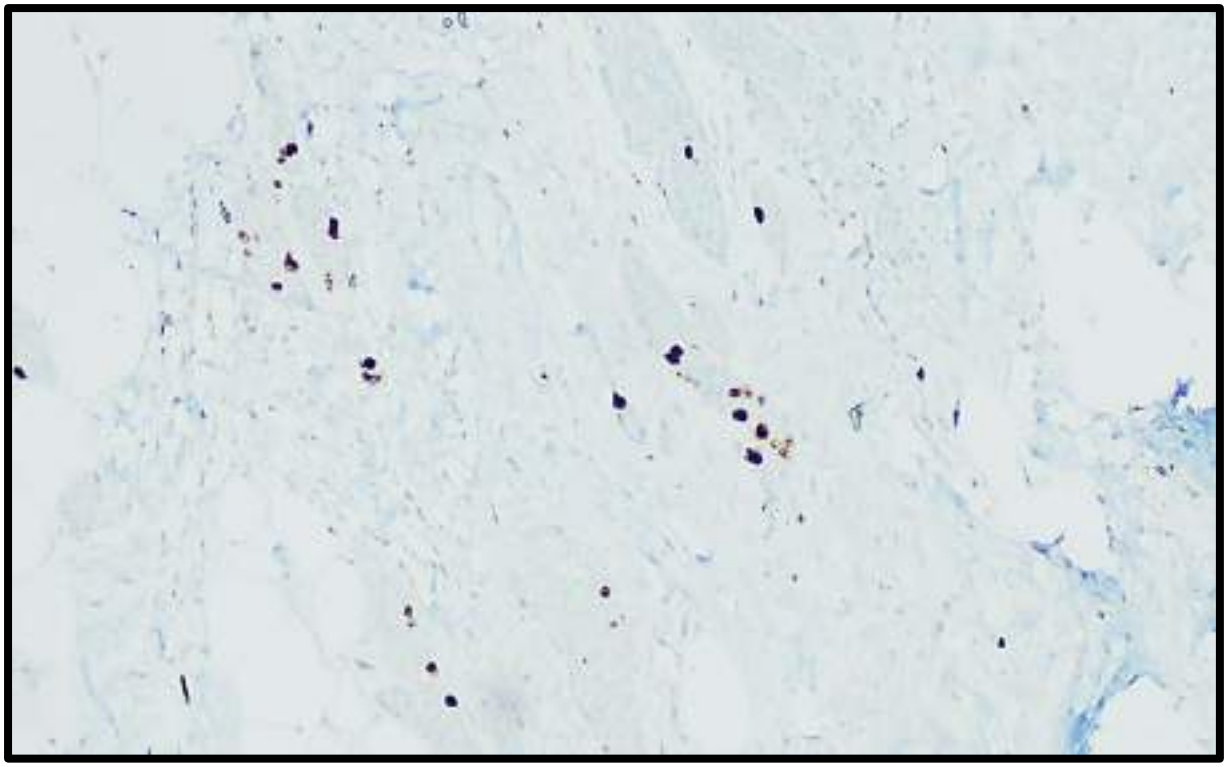
Picture 54- Photomicrograph of HER 2/ neu interpretation = 1+ (Negative), showing incomplete membranous staining that is faint/ barely perceptible and within >10% of the tumor cells (IHC, 100X)



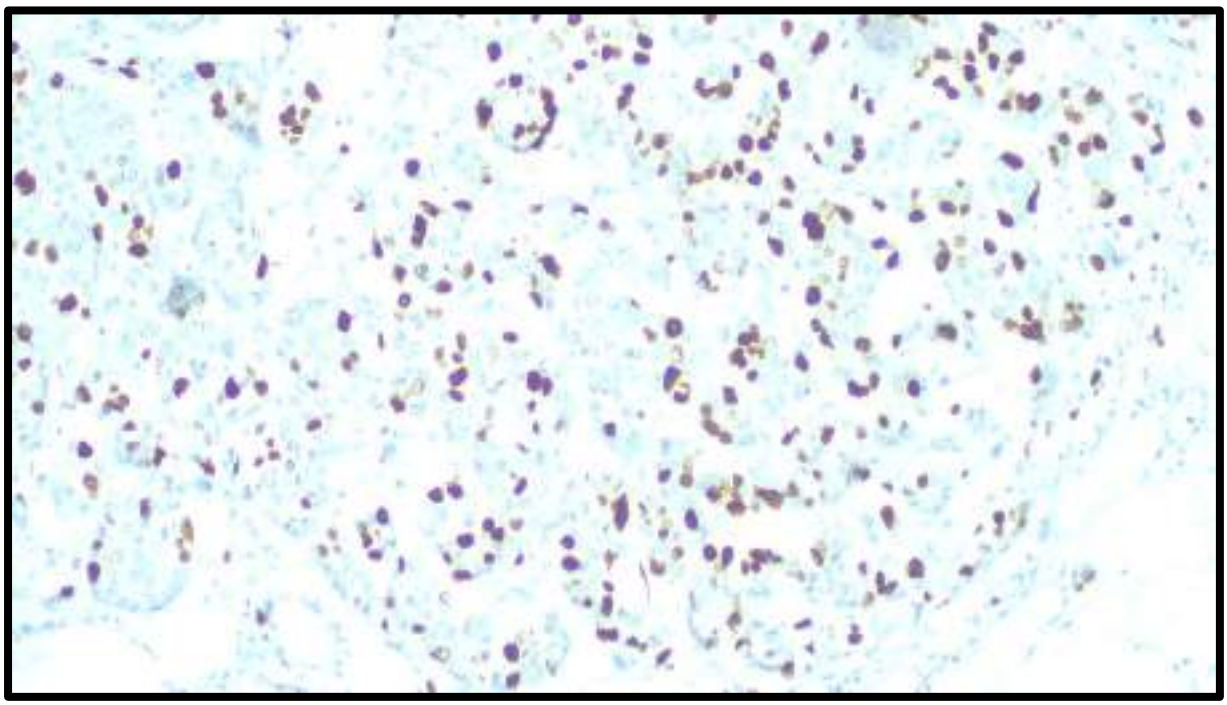
Picture 55- Photomicrograph of HER 2/ neu interpretation = 2+ (Equivocal), showing weak and moderate complete membranous staining in >10% of the tumor cells (IHC, 400X)



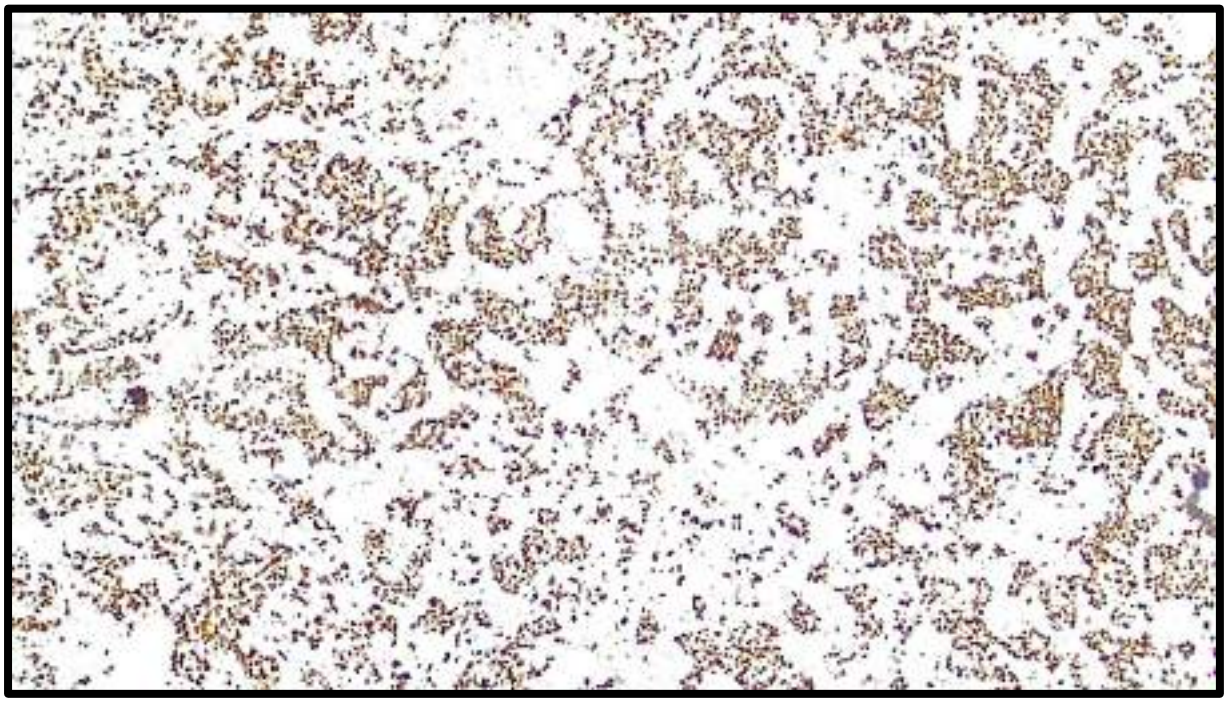
Picture 56- Photomicrograph of HER 2/ neu interpretation = 3+ (Positive), showing complete, intense, circumferential membranous staining within >10% of the tumor cells (IHC, 100X)



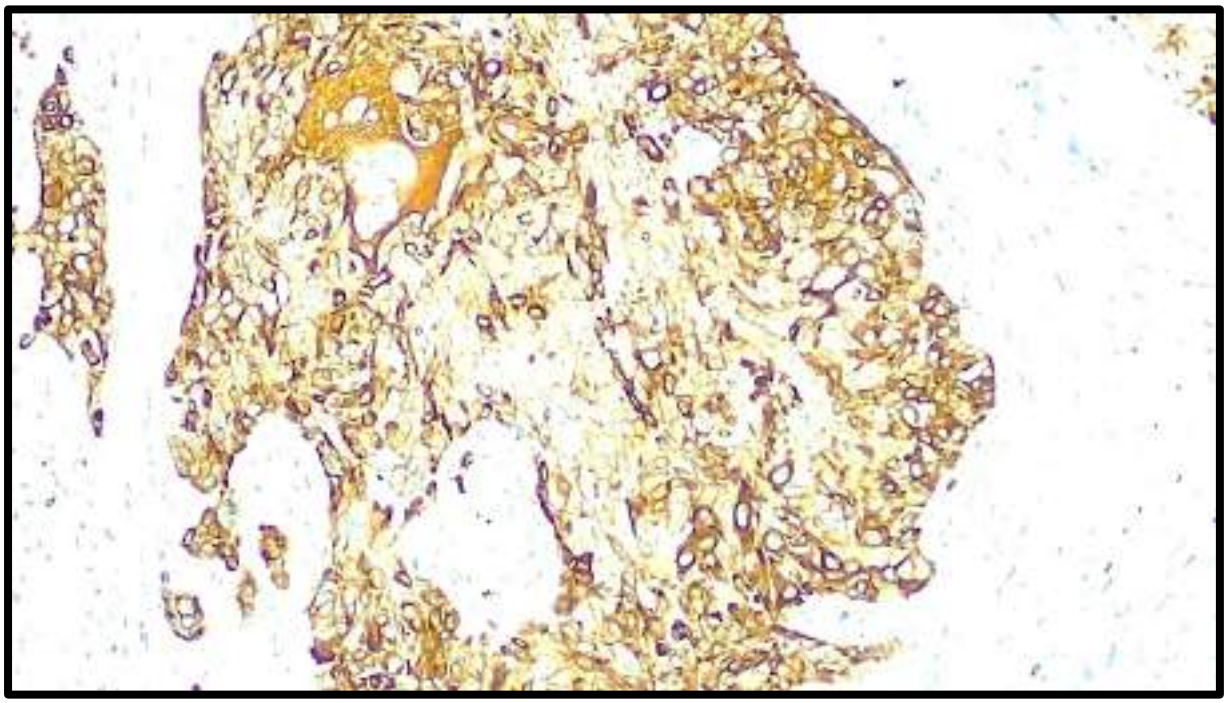
Picture 57- Photomicrograph of Ki-67 in the highest proliferating areas = 12% (IHC, 100X)



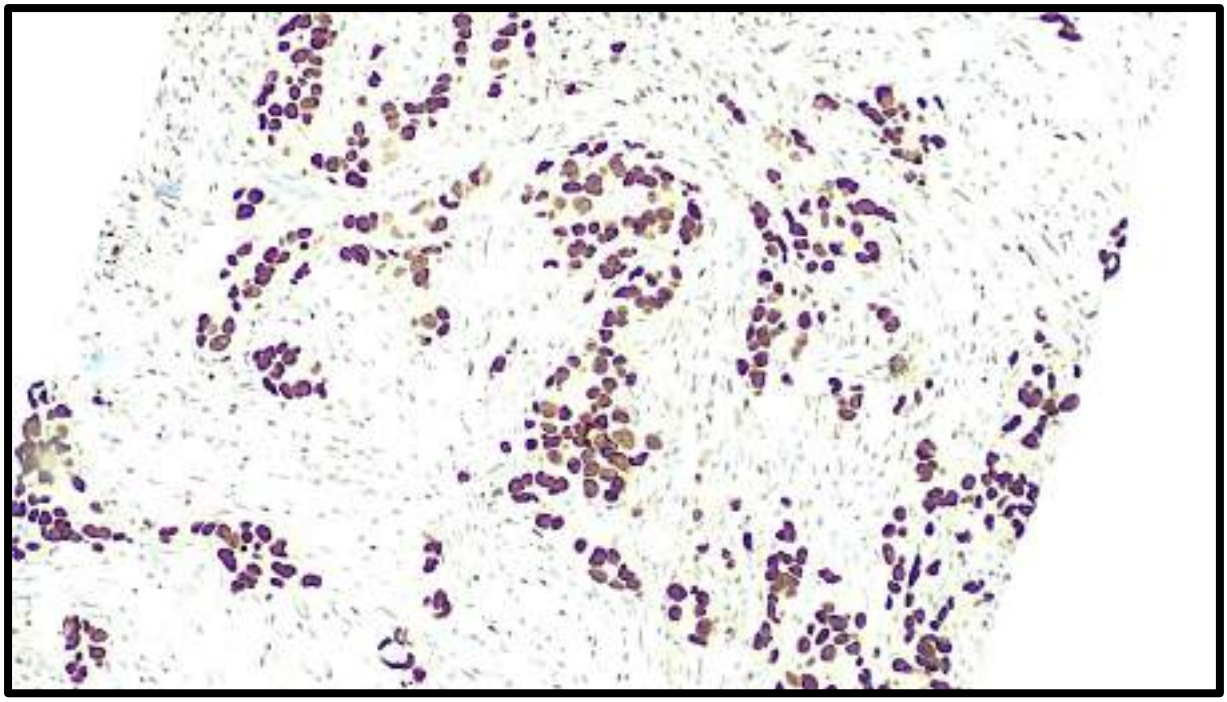
Picture 58- Photomicrograph of Ki-67 in the highest proliferating areas = 30% (IHC, 100X)



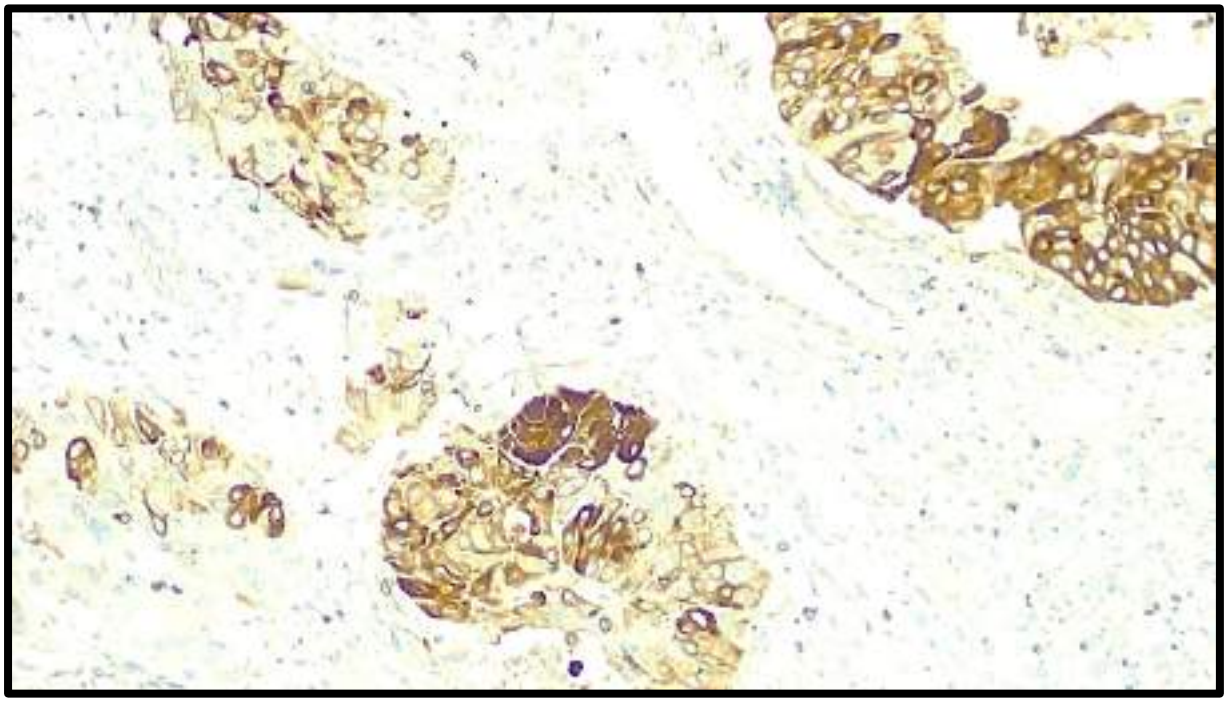
Picture 59- Photomicrograph of Ki-67 in the highest proliferating areas = 95% (IHC, 40X)



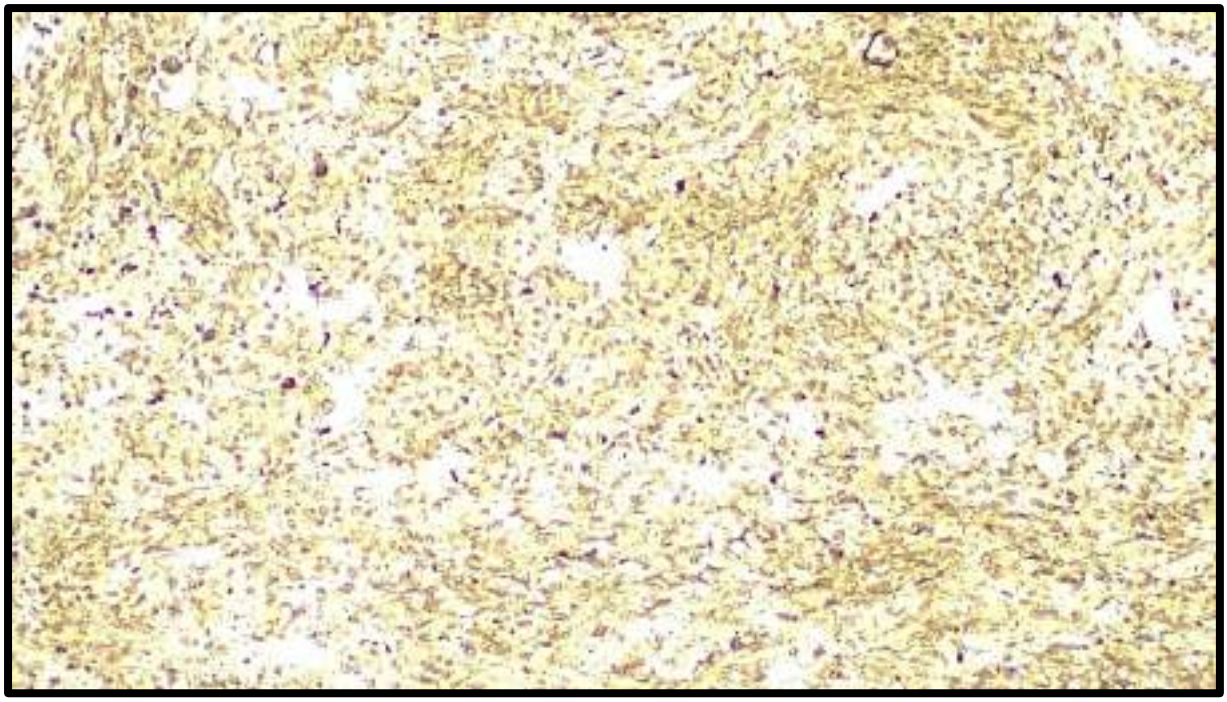
Picture 60- Photomicrograph of immunopositivity of CK 5/6 in Triple negative molecular profile (IHC, 100X)



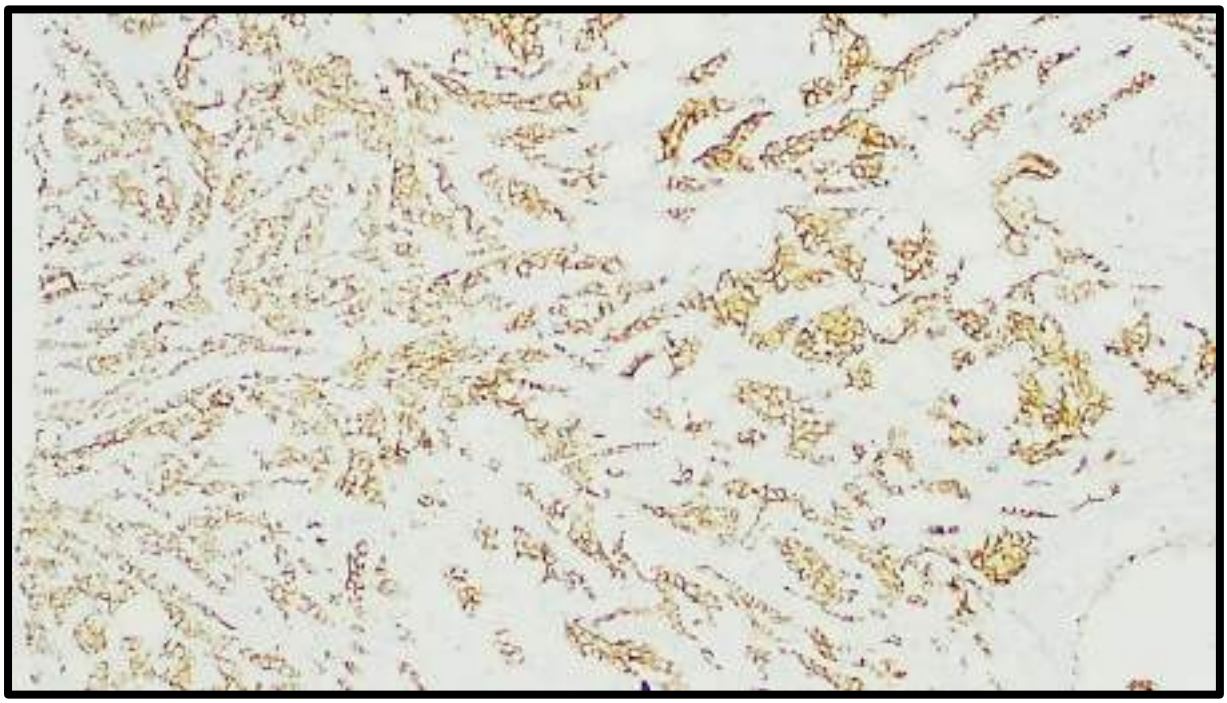
Picture 61- Photomicrograph of immunopositivity of GATA-3 (nuclear expression) (IHC, 100X)



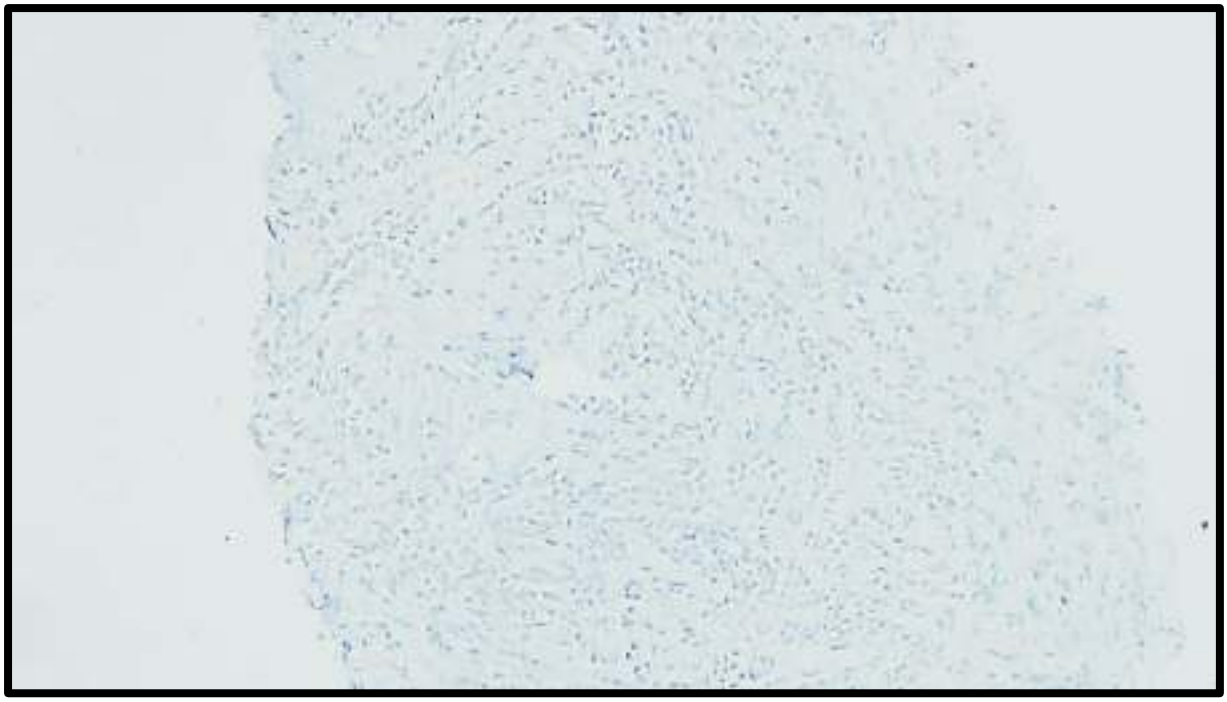
Picture 62- Photomicrograph of immunopositivity of Mammaglobin (cytoplasmic expression) (IHC, 100X)



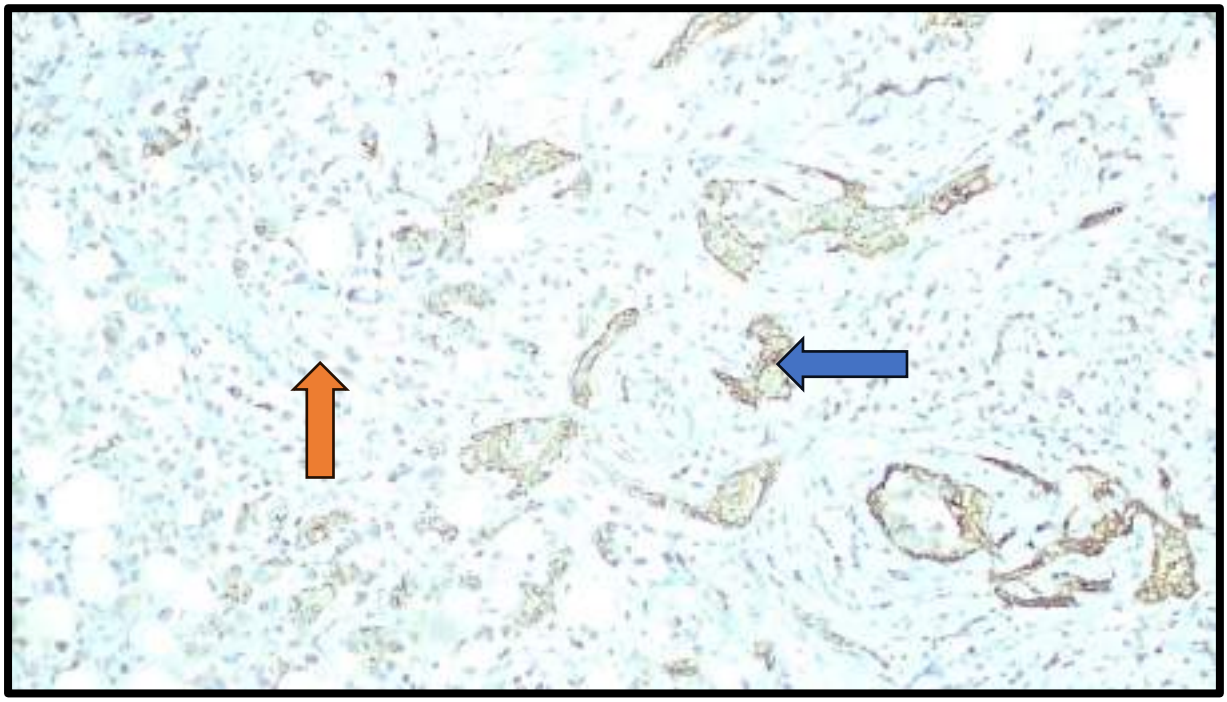
Picture 63- Photomicrograph of immunopositivity of SOX-10 (nuclear expression) (IHC, 40X)



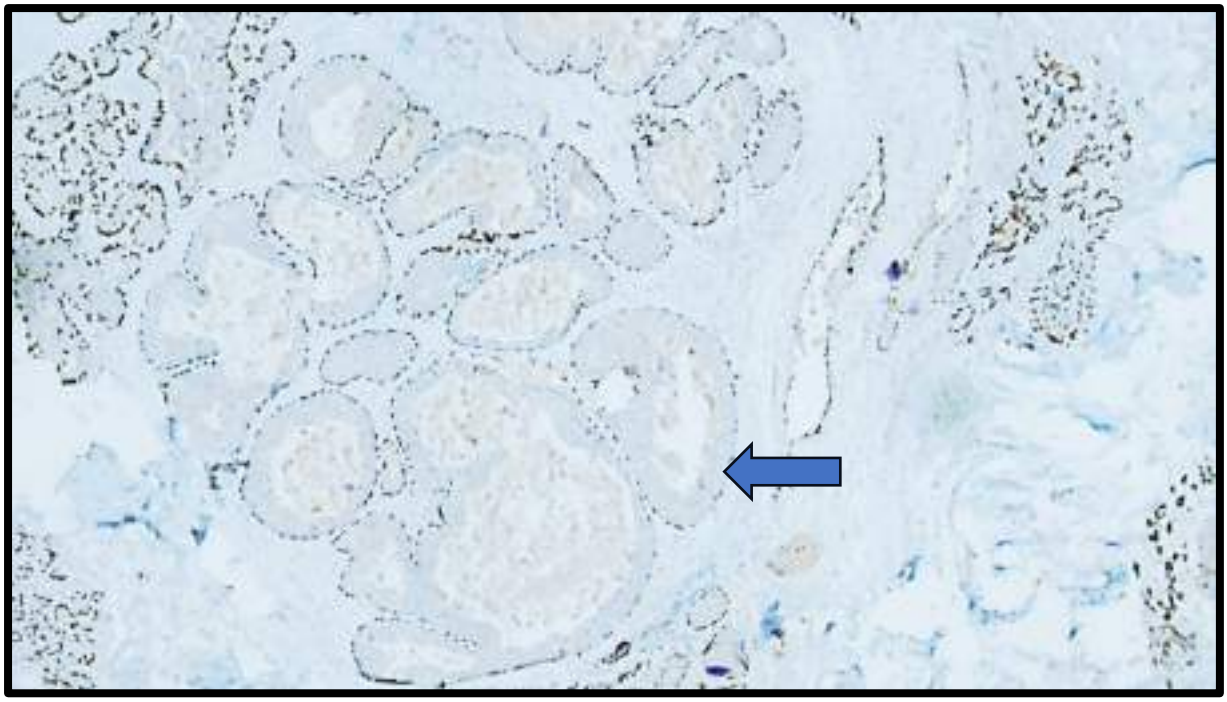
Picture 64- Photomicrograph of interpretation of E-cadherin: Intact (membranous and cytoplasmic expression) (IHC, 100X)



Picture 65- Photomicrograph of interpretation of E-cadherin: Lost (IHC, 100X)



Picture 66- Photomicrograph showing E-cadherin expression in Mixed IDC-NOS (intact; blue arrow) and invasive lobular carcinoma (lost; orange arrow) (IHC, 100X)



Picture 67- Photomicrograph showing p63 immunostaining (nuclear expression) highlighting the myoepithelial cell layerin the ductal component (arrow) (IHC; 40X)

KEY TO MASTER CHART

BCS	Breast conservation surgery
Ca	Carcinoma
cGrade	Clinical grade
cStage	Clinical stage
F	Female
FNAC	Fine needle aspiration cytology
H/o	History of
IDC, NOS	Infiltrating Duct Carcinoma, Not otherwise Specified
L	Left
LCIS	Lobular carcinoma in situ
LI	Lower inner
LN	Lymph node
LO	Lower outer
MBR	Modified Bloom Richardson
N	Node
No.	Number
R	Right
T	Tumor
UO	Upper outer

S. No.	Patient's name	Age	Sex	MRD no.	Histopathology No.	IHC No.	Presented with breast lump	Presented with breast pain/ heaviness	Presented with nipple enlargement/ discharge/ retraction	Duration of symptoms of presenting illness	Personal history	Past history	Family history	Breast laterality	Breast quadrant	cStage	cT	cN	cM	cGrade	Response to chemotherapy
1	AM	59	F	575618	10424/22	1162/22	No	Yes	No	1 month	Post-menopausal	Not significant	Not significant	Left	Lower outer	IIIA	2	3a	0	2	Not applicable
2	RJ	56	F	1381015	10825/22	1182/22	Yes	No	No	15 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
3	KR	38	F	1373201	10770/22	1193/22	Yes	No	No	Not known	Not known	Not significant	Not significant	Left	Not known	IIIB	2	3	0	2	Not applicable
4	SD	52	F	1368040	10574/22	1195/22	Yes	No	No	10-15 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
5	KD	50	F	1375604	10822/22	1196/22	Yes	No	No	Not known	Not known	Not significant	Not significant	Right	Upper inner	IA	2	0	0	2	Not applicable
6	SK	55	F	1379210	11016/22	1221/22	Yes	No	No	1.5-2 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
7	JK	50	F	1385801	11151/22	1224/22	Yes	No	No	7-10 days	Post-menopausal	Not significant	Not significant	Left	Central	IA	2	0	0	2	Not applicable
8	SB	50	F	233121	11020/22	1231/22	Yes	No	No	15 days	Post-menopausal	Not significant	Not significant	Right	Central	IIA	3	1	0	2	Not applicable
9	JK	53	F	551658	11227/22	1238/22	Yes	No	No	3 months	Post-menopausal	Not significant	Not significant	Right	Not known	IIIA	2	2	0	2	Not applicable
10	MG	69	F	1043305	11278/22	1240/22	Yes	No	No	20 days	Post-menopausal	Not significant	Not significant	Left	Upper outer	IIB	2	1	0	Not known	Not applicable
11	RK	60	F	1387501	11319/22	1244/22	Yes	No	No	Not known	Not known	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
12	NJ	38	F	1384934	11478/22	1251/22	Yes	No	No	Not known	Not known	Not significant	Not significant	Left	Lower inner	IV	4d	2	1	2	Not applicable
13	PD	35	F	1385562	11222/22	1248/22	Yes	No	No	1 month	Pre-menopausal	Not significant	Not significant	Left	Lower inner	IB	1	0	0	3	Not applicable
14	B	50	F	1383338	11422/22	1266/22	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Right	Lower outer	IA	2	0	0	2	Not applicable
15	MK	60	F	306466	11892/22	1304/22	No	No	Yes	2 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
16	SR	58	F	564198	11819/22	1305/22	Yes	No	No	Not known	Post-menopausal	Not significant	Not significant	Left	Not known	X	4b	2	1	3	Not applicable
17	KR	66	F	1134257	11781/22	1309/22	Yes	No	No	1.5 months	Post-menopausal	Not significant	Not significant	Left	Lower inner	IIB	2	1a	0	2	Not applicable
18	JK	53	F	1391466	11752/22	1317/22	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
19	RK	75	F	119962	11931/22	1319/22	Yes	No	No	15 days	Post-menopausal	Not significant	Not significant	Left	Upper outer	Not known	Not known	Not known	Not known	Not known	Not applicable
20	KK	34	F	1377490	10558/22	1331/22	Yes	No	No	Not known	Not known	Not significant	Not significant	Right	Upper outer	Not known	Not known	Not known	Not known	Not known	Not applicable
21	PC	65	F	1396683	12075/22	1336/22	Yes	No	No	4 months	Post-menopausal	Not significant	Not significant	Right	Upper outer	IB	3	0	0	2	Not applicable
22	SR	54	F	1401266	12224/22	1338/22	Yes	No	No	25 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
23	PL	72	F	167270	12068/22	1344/22	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Left	Central	IIIC	2	3a	0	3	Not applicable
24	MK	38	F	1404104	12396/22	1351/22	Yes	No	No	Not known	Not known	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
25	VR	44	F	7463	12394/22	1364/22	Yes	No	No	7 days	Post-menopausal	Not significant	Not significant	Right	Upper inner	IIA	Not known	Not known	Not known	Not known	Not applicable
26	SK	61	F	1396304	12607/22	1384/22	Yes	No	No	Not known	Post-menopausal	Not significant	Not significant	Right	Lower outer	X	2	3	0	3	Not applicable
27	P	87	F	1379995	10844/22	1389/22	Yes	No	No	3 months	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
28	KJ	64	F	1401195	12530/22	1390/22	Yes	No	No	20 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
29	RA	47	F	1406843	12637/22	1391/22	Yes	No	No	1.5 months	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable

S. No.	Mammography/ USG BIRADS	Evidence of metastasis in CT scan	PET scan findings/ LN metastasis	Pleural Fluid	FNAC (if any)	Types of specimens	Status of overlying skin	Nipple retracted	Growth	No. of lesions	Size of growth	Distance from overlying skin (in cms)	Histopathological type	MBR grade	T	Grade of DCIS	Percentage of tumor area	Papillary Pattern DCIS	Micropapillary pattern DCIS	Solid pattern DCIS	Comedo pattern DCIS	Cribriform pattern DCIS	LCIS
1	IV	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.8X2X1.5 cms	0.5	IDC, NOS	II	2	Intermediate	25	Present	Absent	Present	Present	Absent	Absent
2	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
3	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.5X2.8X1.5 cms	1.3	IDC, NOS	II	2	Absent	10	Absent	Present	Absent	Absent	Absent	Absent
4	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.2X1.8X1.5 cms	1	IDC, NOS	II	2	Intermediate	5	Absent	Absent	Absent	Present	Absent	Absent
5	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.5X3X2 cms	2.5	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
6	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	1.7X1.2X1 cms	2	IDC, NOS	II	1	High	10	Absent	Absent	Present	Present	Absent	Absent
7	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
8	V	Not known	Not known	Not known	Carcinoma (category V Yokohama)	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent
9	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.4X3.8X1.5 cms	1.5	IDC, NOS	II	2	Intermediate	10	Absent	Present	Absent	Present	Present	Absent
10	V	Not known	Not known	Not known	Left axillary LN: Reactive hyperplasia	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
11	Not known	Not known	Not known	Not known	Carcinoma (category V Yokohama)	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
12	V	Bony metastasis present	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
13	IV	No evidence	No evidence of metastatic disease	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	1.8X1.5X1.3 cms	2.5	IDC, NOS	III	1	High	90	Absent	Absent	Present	Present	Present	Absent
14	BIRADS not mentioned	Not known	Not known	Not known	Carcinoma (category V Yokohama)	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.3X2.5X2.1 cms	1.2	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
15	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Absent	Not applicable	Not applicable	Not applicable	IDC, NOS	II	1	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
16	Not known	Not known	Not known	Not known	Carcinoma (category V Yokohama)	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
17	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.2X4X3.2 cms	2.5	IDC, NOS	II	2	High	5	Absent	Absent	Absent	Absent	Present	Absent
18	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	5X2.2X2 cms	1	IDC, NOS	II	3	Intermediate	10	Absent	Absent	Absent	Present	Absent	Absent
19	Not known	Likely pulmonary metastasis present	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.5X2.8X1.8 cms	2	IDC, NOS	III	2	High	5	Absent	Absent	Absent	Present	Absent	Absent
20	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Multiple	3.4X2.5X1.8 cms	2.3	IDC, NOS	II	2	Intermediate	5	Absent	Absent	Present	Present	Absent	Absent
21	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	5.2X3.5X2.6 cms	1.6	IDC, NOS	II	3	Intermediate	10	Absent	Absent	Present	Absent	Present	Absent
22	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
23	BIRADS not mentioned	Possibility of residual disease not completely ruled out	Possibility of residual disease not completely ruled out	Not known	Additional sampling recommended	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
24	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
25	IVc	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.2X3.5X2.2 cms	1.6	IDC, NOS	III	2	Intermediate	20	Absent	Absent	Present	Absent	Present	Absent
26	V	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.8X3X2 cms	1.2	IDC, NOS	II	2	Intermediate	40	Absent	Absent	Present	Present	Absent	Absent
27	IV	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	Yes	Present	Solitary	1.5X1.2X0.9 cms	1.4	IDC, NOS	II	1	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
28	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.5X3X2 cms	1	IDC, NOS	II	2	Intermediate	5	Absent	Absent	Present	Absent	Absent	Absent
29	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.8X3.5X2.9 cms	1	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

S. No.	Tumor necrosis	Skin invasion	Lymphovascular invasion	Microcalcifications	Tumor margins	Lymphocytic response at the advancing margins	Perineural invasion	Deep resected margin	Skeletal muscle involvement	Regional lymph nodes positive for metastasis	Total no. of regional lymph nodes	Sentinel lymph nodes positive for metastasis	Total no. of sentinel lymph nodes	Level 3 lymph nodes positive for metastasis	Total no. of level 3 lymph nodes	Total no. of positive lymph nodes	Total no. of lymph nodes examined	N	Extranodal Extension	Treatment induced changes in breast	ER (out of 8)
1	Absent	Absent	Present	Present	Infiltrating	No significant response	Absent	Free	Absent	15	23	Not recovered	Not recovered	Not recovered	Not recovered	15	23	3	Present	Not seen	8
2	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
3	Absent	Absent	Absent	Absent	Infiltrating	Moderate	Absent	Free	Absent	Nine	20	Not recovered	Not recovered	Three	10	Twelve	30	3	Present	Not seen	0
4	Present	Absent	Present	Absent	Infiltrating	Mild	Present	Free	Absent	17	29	Not recovered	Not recovered	Seven	8	24	37	3	Present	Not seen	0
5	Present	Absent	Absent	Absent	Infiltrating	Moderate	Absent	Free	Absent	0	23	Not recovered	Not recovered	0	6	0	29	0	Absent	Not seen	8
6	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	12	Not recovered	Not recovered	0	6	0	18	0	Absent	Not seen	8
7	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	8	Not recovered	Not recovered	Not recovered	Not recovered	0	8	0	Absent	Not seen	8
8	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
9	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	nineteen	Two	4	0	8	2	31	2	Present	Not seen	0
10	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	2
11	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
12	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
13	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	19	Not recovered	Not recovered	0	6	0	25	0	Absent	Not seen	0
14	Absent	Absent	Absent	Present	Infiltrating	Mild	Absent	Free	Absent	0	13	Not recovered	Not recovered	0	1	0	14	0	Absent	Not seen	8
15	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	0	17	Not recovered	Not recovered	0	2	0	19	0	Absent	Not seen	8
16	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
17	Present	Absent	Present	Absent	Infiltrating	Mild	Absent	Free	Absent	1	15	Not recovered	Not recovered	0	1	1	16	1	Present	Not seen	0
18	Absent	Absent	Absent	Absent	Infiltrating	Moderate	Absent	Free	Absent	2	20	Not recovered	Not recovered	1	2	3	22	1	Absent	Not seen	0
19	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	3	19	Not recovered	Not recovered	0	5	3	24	1	Absent	Not seen	0
20	Absent	Absent	Absent	Absent	Infiltrating	Moderate	Absent	Free	Absent	0	9	Not recovered	Not recovered	Not recovered	Not recovered	0	9	0	Absent	Not seen	4
21	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	30	Not recovered	Not recovered	0	8	0	38	0	Absent	Not seen	8
22	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
23	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
24	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
25	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	24	Not recovered	Not recovered	0	10	0	34	0	Absent	Not seen	6
26	Present	Absent	Present	Present	Infiltrating	Mild	Absent	Free	Absent	13	14	Not recovered	Not recovered	Not recovered	Not recovered	13	14	3	Present	Not seen	8
27	Absent	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Absent	0	16	Not recovered	Not recovered	Not recovered	Not recovered	0	16	0	Absent	Not seen	8
28	Absent	Absent	Absent	Present	Infiltrating	Mild	Absent	Free	Absent	0	3	0	3	Not recovered	Not recovered	0	3	0	Absent	Not seen	8
29	Present	Absent	Present	Present	Infiltrating	Moderate	Absent	Free	Absent	6	27	Not recovered	Not recovered	0	4	6	31	2	Absent	Not seen	0

S. No.	PR (out of 8)	HER 2/ neu	FISH analysis (in case of equivocal HER 2/ neu)	Ki-67 Percentage of Positive Nuclei	Additional marker E-cadherin	Additional marker EMA	Additional marker CK	Additional marker p63	Additional marker Mammaglobin	Additional marker p40	Additional marker Vimentin	Additional marker SMA	Additional marker 34BE12	Additional marker Synaptophysin	Additional marker Chromogranin A	Additional marker CK 5/6	Additional marker SOX-10	Additional marker GATA-3	Molecular Subtype
1	6	Positive	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
2	0	Negative	Not applicable	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Diffuse moderate positive	Triple Negative
3	0	Positive	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
4	0	Positive	Not applicable	85	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
5	6	Negative	Not applicable	65	Intact	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
6	6	Negative	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
7	8	Negative	Not applicable	25	Intact	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
8	8	Negative	Not applicable	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
9	0	Positive	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
10	0	Positive	Not applicable	85	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
11	8	Negative	Not applicable	Absent	Intact	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
12	8	Negative	Not applicable	30	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
13	0	Negative	Not applicable	40	Absent	Absent	Absent	Negative around tumor cells	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Focal weak positive	Diffuse moderate positive	Triple Negative
14	8	Negative	Not applicable	20	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
15	8	Negative	Not applicable	35	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
16	0	Positive	Not applicable	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
17	0	Negative	Not applicable	75	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Focal strong positive	Absent	Diffuse strong positive	Triple Negative
18	0	Equivocal	Negative	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse moderate positive	Diffuse strong positive	Triple Negative
19	0	Equivocal	Negative	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse moderate positive	Diffuse strong positive	Triple Negative
20	5	Positive	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Triple Negative
21	8	Equivocal	Negative	30	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
22	8	Positive	Not applicable	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
23	0	Negative	Not applicable	35	Absent	Absent	Positive	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Diffuse strong positive	Triple Negative
24	0	Equivocal	Negative	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Diffuse moderate positive	Triple Negative
25	0	Positive	Not applicable	85	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
26	7	Equivocal	Negative	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
27	8	Negative	Not applicable	14	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-A
28	8	Negative	Not applicable	12	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-A
29	0	Positive	Not applicable	75	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched

S. No.	Patient's name	Age	Sex	MRD no.	Histopathology No.	IHC No.	Presented with breast lump	Presented with breast pain/ heaviness	Presented with nipple enlargement/ discharge/ retraction	Duration of symptoms of presenting illness	Personal history	Past history	Family history	Breast laterality	Breast quadrant	cStage	cT	cN	cM	cGrade	Response to chemotherapy
30	PL	72	F	167270	12635/22	1392/22	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
31	RS	59	F	1406204	12595/22	1394/22	Yes	No	No	7 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
32	KK	43	F	1396192	12633/22	1395/22	Yes	No	No	10 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
33	Pk	52	F	1335212	12809/22	1411/22	No	Yes	No	12-15 days	Post-menopausal	Not significant	Not significant	Left	Lower outer	IIB	2	1	0	2	Present
34	HK	57	F	1409870	12893/22	1413/22	Yes	No	No	2.5 months	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
35	SJ	71	F	1404629	12902/22	1414/22	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
36	RS	71	F	1399362	12293/22	1417/22	Yes	No	No	3 months	Post-menopausal	Not significant	Not significant	Left	Upper outer	IB	2	0	0	3	Not applicable
37	SB	52	F	1412966	13049/22	1420/22	Yes	No	No	Not known	Not known	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
38	BK	66	F	1316717	12353/22	1424/22	Yes	No	No	10 days	Post-menopausal	Not significant	Not significant	Bilateral	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
39	AT	70	F	1414430	13111/22	1440/22	Yes	No	No	15 days	Parity: 2	Not significant	H/o Ca breast in 2 sisters and 1 aunt	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
40	AK	55	F	1415615	13233/22	1441/22	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
41	AM	68	F	1049255	12733/22	1444/22	Yes	No	No	3-4 months	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
42	SS	50	F	1412278	12983/22	1446/22	Yes	No	No	5-6 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
43	GK	60	F	1410701	12844/22	1447/22	Yes	No	No	15 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
44	BK	62	F	1414248	13164/22	1448/22	Yes	No	No	7-10 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
45	MD	54	F	1410039	12872/22	1459/22	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
46	AS	44	F	1393632	12357/22	1467/22	Yes	No	No	20 days	Post-menopausal	Not significant	Not significant	Left	Upper inner	IA	2	0	0	2	Not applicable

S. No.	Mammography/ USG BIRADS	Evidence of metastasis in CT scan	PET scan findings/ LN metastasis	Pleural Fluid	FNAC (if any)	Types of specimens	Status of overlying skin	Nipple retracted	Growth	No. of lesions	Size of growth	Distance from overlying skin (in cms)	Histopathological type	MBR grade	T	Grade of DCIS	Percentage of tumor area	Papillary Pattern DCIS	Micropapillary pattern DCIS	Solid pattern DCIS	Comedo pattern DCIS	Cribriform pattern DCIS	LCIS
30	Not known	Not known	Not known	Not known	Additional sampling recommended	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
31	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.5X3X2 cms	1.2	IDC, NOS	I	2	Intermediate	70	Absent	Absent	Present	Present	Absent	Absent
32	Not known	Not known	Not known	Not known	Not known	Breast Conservation Surgery (BCS)	Normal	Not applicable	Present	Solitary	2.2X1.8X1.5 cms	1.5	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
33	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
34	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3X2.8X1.8 cms	2	IDC, NOS	III	2	High	85	Absent	Absent	Present	Present	Absent	Absent
35	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	5.1X4.5X3 cms	1.3	Metaplastic carcinoma	III	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
36	IVc	No evidence	FDG avid mass upper outer quadrant of L breast with enlarged LNs	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.8X4X4 cms	0.1	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
37	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
38	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	Not applicable	Not applicable	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
39	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	1.2X1.1X0.8 cms	1.7	IDC, NOS	II	1	Intermediate	15	Absent	Absent	Present	Present	Absent	Absent
40	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
41	Not known	Not known	Not known	Not known	Carcinoma (category V Yokohama)	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	I	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
42	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4X3X3 cms	1	IDC, NOS	II	2	Intermediate	20	Absent	Absent	Absent	Present	Absent	Absent
43	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	1X0.8X0.3 cms	2.7	IDC, NOS	II	1	Intermediate	20	Absent	Absent	Absent	Absent	Present	Absent
44	Not known	Not known	Not known	Not known	Not known	Lumpectomy/ Excision	Normal	Not applicable	Haemorrhagic cystic area present	Solitary	1.5X1X0.5 cms	1	IDC, NOS	III	1	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
45	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.1X2X1.5 cms	1.5	IDC, NOS	II	2	High	20	Absent	Absent	Present	Present	Absent	Absent
46	Not known	No evidence	Focal FDG avid enhancing lesion upper inner quadrant L breast- likely malignant primary disease. FDG avid lesion bulky right adnexal region- may be physiological. No other abnormal FDG avid lesion seen in rest of the body region surveyed.	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.2X2X1.8 cms	1.5	IDC, NOS	II	2	High	5	Absent	Absent	Present	Present	Absent	Absent

S. No.	Tumor necrosis	Skin invasion	Lymphovascular invasion	Microcalcifications	Tumor margins	Lymphocytic response at the advancing margins	Perineural invasion	Deep resected margin	Skeletal muscle involvement	Regional lymph nodes positive for metastasis	Total no. of regional lymph nodes	Sentinel lymph nodes positive for metastasis	Total no. of sentinel lymph nodes	Level 3 lymph nodes positive for metastasis	Total no. of level 3 lymph nodes	Total no. of positive lymph nodes	Total no. of lymph nodes examined	N	Extranodal Extension	Treatment induced changes in breast	ER (out of 8)
30	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
31	Absent	Absent	Present	Present	Infiltrating	Mild	Absent	Free	Absent	5	17	3	4	0	5	8	28	2	Absent	Not seen	8
32	Present	Absent	Present	Absent	Infiltrating	Moderate	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Present	Not seen	0
33	Absent	Absent	Absent	Present	Pushing	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
34	Present	Absent	Present	Present	Infiltrating	Mild	Absent	Free	Absent	1	19	Not recovered	Not recovered	Not recovered	Not recovered	1	19	1	Present	Not seen	0
35	Present	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	9	0	9	Not recovered	Not recovered	0	18	0	Absent	Not seen	0
36	Present	Absent	Absent	Absent	Infiltrating	Mild	Present	Free	Absent	0	21	Not recovered	Not recovered	0	4	0	25	0	Absent	Not seen	8
37	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
38	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	7	18	Not recovered	Not recovered	Not recovered	Not recovered	7	18	2	Absent	Not seen	8
39	Absent	Absent	Absent	Present	Infiltrating	Mild	Absent	Free	Absent	0	12	0	2	Not recovered	Not recovered	0	14	0	Absent	Not seen	8
40	Present	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	4
41	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
42	Absent	Absent	Present	Present	Infiltrating	No significant response	Absent	Free	Absent	8	15	Not recovered	Not recovered	Not recovered	Not recovered	8	15	2	Present	Not seen	8
43	Absent	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Absent	17	17	Not recovered	Not recovered	2	2	19	19	3	Present	Not seen	8
44	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
45	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	12	Not recovered	Not recovered	Not recovered	Not recovered	0	12	0	Absent	Not seen	8
46	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	15	Not recovered	Not recovered	0	5	0	20	0	Absent	Not seen	8

S. No.	PR (out of 8)	HER 2/ neu	FISH analysis (in case of equivocal HER 2/ neu)	Ki-67 Percentage of Positive Nuclei	Additional marker E-cadherin	Additional marker EMA	Additional marker CK	Additional marker p63	Additional marker Mammaglobin	Additional marker p40	Additional marker Vimentin	Additional marker SMA	Additional marker 34BE12	Additional marker Synaptophysin	Additional marker Chromogranin A	Additional marker CK 5/6	Additional marker SOX-10	Additional marker GATA-3	Molecular Subtype
30	0	Equivocal	Negative	Absent	Absent	Absent	Positive	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Focal strong positive	Absent	Focal weak positive	Triple Negative
31	8	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
32	0	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse moderate positive	Diffuse strong positive	Triple Negative
33	0	Negative	Not applicable	35	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
34	0	Positive	Not applicable	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
35	0	Equivocal	Negative	70	Absent	Absent	Absent	Absent	Positive	Focal positive	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Diffuse strong positive	Triple Negative
36	8	Negative	Not applicable	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
37	8	Negative	Not applicable	10	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-A
38	0	Negative	Not applicable	8	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-A
39	6	Positive	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
40	4	Positive	Not applicable	30	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
41	5	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
42	8	Equivocal	Negative	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Focal weak positive	Triple Negative
43	8	Equivocal	Negative	30	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
44	6	Equivocal	Negative	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Diffuse moderate positive	Triple Negative
45	5	Negative	Not applicable	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
46	8	Negative	Not applicable	12	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-A

S. No.	Patient's name	Age	Sex	MRD no.	Histopathology No.	IHC No.	Presented with breast lump	Presented with breast pain/ heaviness	Presented with nipple enlargement/ discharge/ retraction	Duration of symptoms of presenting illness	Personal history	Past history	Family history	Breast laterality	Breast quadrant	cStage	cT	cN	cM	cGrade	Response to chemotherapy
47	SM	47	F	1417275	13326/22	1475/22	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Lower outer	IIA	2	0	0	2	Not applicable
48	HK	69	F	1422754	13721/22	1493/22	Yes	No	No	3-4months	Post-menopausal	Not significant	Not significant	Right	Upper inner	IV	2	1	1	X	Not applicable
49	HK	80	F	1353008	13572/22	1482/22	Yes	No	No	2.5 months	Post-menopausal	Not significant	Not significant	Right	Lower outer	IIIC	4	1	0	3	Not applicable
50	UL	63	F	1420894	13671/22	1498/22	Yes	No	No	7 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
51	SK	85	F	1416971	13770/22	1500/22	Yes	No	No	20 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
52	K	45	F	1418036	13507/22	1506/22	Yes	No	No	1.5-2 months	Post-menopausal	Not significant	Not significant	Left	Not known	IIIA	2	3	0	2	Not applicable
53	RS	70	F	1418905	13585/22	1510/22	Yes	No	No	2 months	Parity: 1	Not significant	Not significant	Left	Not known	IIIA	1c	3a	0	1	Not applicable
54	AR	50	F	1426450	13917/22	1514/22	Yes	No	No	2.5 months	Post-menopausal; Parity:4	Not significant	Not significant	Right	Upper, lower, retroareolar and periareolar	X	4b	3c	1	3	Not applicable
55	GK	55	F	1423672	13901/22	1539/22	Yes	No	No	1.5-2 months	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
56	NB	37	F	1424858	14019/22	1544/22	Yes	No	No	Not known	Not known	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
57	GK	59	F	1428381	14107,14098,14099,14100/22	1547/22	Yes	No	No	20 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
58	CK	62	F	1428922	14293/22	1553/22	Yes	No	No	25 days	Post-menopausal	Not significant	Not significant	Right	Upper outer	X	2	2	1	2	Not applicable
59	MJ	47	F	525443	14256/22	1558/22	Yes	No	No	10-15 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
60	KK	47	F	1428388	O/S Block 22L-234 A	1560/22	NA	NA	NA	Not known	Not known	Not significant	Not significant	Right	Lower outer	Not known	Not known	Not known	Not known	Not known	Not applicable
61	KK	69	F	1425552	13989/22	1562/22	Yes	No	No	2 months	Not known	Not significant	Not significant	Right	Retroareolar	IIA	2	0	0	2	Not applicable
62	PK	68	F	1428352	14370/22	1563/22	Yes	No	No	1.5-2 months	Post-menopausal	Not significant	Not significant	Left	Not known	X	2	0	0	2	Not applicable
63	GK	51	F	1422825	13987/22	1570/22	Yes	No	No	25 days	Post-menopausal	Not significant	Not significant	Right	Upper outer	IIIA	3	3a	0	2	Not applicable
64	JK	47	F	1431632	14584/22	1576/22	Yes	No	No	3 months	Pre-menopausal	Not significant	H/o malignancy in cousin	Right	Not known	X	2	0	0	3	Not applicable
65	M	43	F	1436431	14683/22	1578/22	Yes	No	No	1.5-2 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
66	SR	68	F	1433964	14682/22	1587/22	Yes	No	No	10 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
67	PK	57	F	1425490	14802/22	1/23	Yes	No	Yes	2 months	Post-menopausal; Parity: 2; Intake of OCPs: Absent	Not significant	Not significant	Left	Upper outer	IIIA	2	3	0	2	Not applicable

S. No.	Mammography/ USG BIRADS	Evidence of metastasis in CT scan	PET scan findings/ LN metastasis	Pleural Fluid	FNAC (if any)	Types of specimens	Status of overlying skin	Nipple retracted	Growth	No. of lesions	Size of growth	Distance from overlying skin (in cms)	Histopathological type	MBR grade	T	Grade of DCIS	Percentage of tumor area	Papillary Pattern DCIS	Micropapillary pattern DCIS	Solid pattern DCIS	Comedo pattern DCIS	Cribriform pattern DCIS	LCIS
47	V	No evidence	Low grade FDG avid parenchymal and overlying skin left breast with subpleural lung lesions likely post-treatment inflammatory changes. No other abnormal FDG avid lesion seen in rest of the body region surveyed.	Not known	Carcinoma (category V Yokohama)	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
48	V	Lytic lesions in C4, D4 and D12	FDG avid lesion in upper-inner quadrant of R breast with FDG avid R axillary LNs. FDG avid lytic lesion C4, D4 and D12.	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Invasive Lobular carcinoma	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
49	Not known	No evidence	Post surgical seroma and inflammatory changes right chest wall	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
50	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.5X1.5X1.5 cms	2	IDC, NOS	II	2	Absent	20	Absent	Absent	Present	Present	Absent	Absent
51	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4X3X2 cms	2	IDC, NOS	III	2	Intermediate	15	Absent	Absent	Present	Present	Present	Absent
52	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Not known	Not known	Present	Solitary	4.5X4X1 cms	1.5	IDC, NOS	II	2	High	25	Absent	Present	Present	Present	Absent	Absent
53	Not known	No evidence	Positive axillary lymph nodes	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	1.8X1.5X1.2 cms	2.8	IDC, NOS	I	1	High	25	Absent	Absent	Present	Present	Present	Absent
54	Not known	Not known	Right breast lesion; enlarged R axillary LNs	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
55	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3X2.8X2.5 cms	1.2	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
56	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
57	Not known	Not known	Not known	Not known	Not known	Total mastectomy without axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	III	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
58	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
59	Not known	Not known	Not known	Not known	Not known	Breast Conservation Surgery (BCS)	Normal	Not applicable	Present	Solitary	2.1X1.5X1 cms	4.5	IDC, NOS	III	2	Intermediate	10	Absent	Absent	Present	Present	Absent	Absent
60	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	II	1	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
61	Not known	No evidence	No evidence	Not known	Carcinoma (category V Yokohama)	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.5X1.6X1.5 cms	0.8	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
62	Not known	Not known	Not known	Not known	Not known	Total mastectomy without axillary dissection	Normal	No	Present	Solitary	2.1X1.8X1.5 cms	0.5	IDC, NOS	II	2	Intermediate	15	Absent	Absent	Absent	Present	Present	Absent
63	VI	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	6.5X3X2 cms	1	Invasive Lobular carcinoma	II	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
64	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4X4X2.5 cms	1	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
65	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
66	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
67	V	No evidence	No evidence	Not known	Not known	Total mastectomy+Axillary dissection	Normal	Yes	Present	Solitary	3X2X1.2 cms	1	IDC, NOS	II	2	Absent	10	Present	Present	Present	Absent	Present	Absent

S. No.	Tumor necrosis	Skin invasion	Lymphovascular invasion	Microcalcifications	Tumor margins	Lymphocytic response at the advancing margins	Perineural invasion	Deep resected margin	Skeletal muscle involvement	Regional lymph nodes positive for metastasis	Total no. of regional lymph nodes	Sentinel lymph nodes positive for metastasis	Total no. of sentinel lymph nodes	Level 3 lymph nodes positive for metastasis	Total no. of level 3 lymph nodes	Total no. of positive lymph nodes	Total no. of lymph nodes examined	N	Extranodal Extension	Treatment induced changes in breast	ER (out of 8)
47	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
48	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
49	Present	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
50	Absent	Absent	Absent	Absent	Infiltrating	Moderate	Present	Free	Absent	0	18	Not recovered	Not recovered	Not recovered	Not recovered	0	18	0	Absent	Not seen	8
51	Present	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Absent	0	14	Not recovered	Not recovered	0	1	0	15	0	Absent	Not seen	0
52	Present	Absent	Present	Present	Infiltrating	No significant response	Absent	Free	Not seen	30	31	Not recovered	Not recovered	6	6	36	37	3	Present	Not seen	8
53	Absent	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Absent	12	17	Cervical LNs present (Level 4 & 5): 0	8	0	4	12	29	3	Present	Not seen	8
54	Absent	Absent	Present	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
55	Absent	Absent	Absent	Absent	Infiltrating	Marked	Absent	Free	Absent	0	25	0	5	Not recovered	Not recovered	0	30	0	Absent	Not seen	0
56	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	13	15	Not recovered	Not recovered	12	12	25	27	3	Absent	Not seen	8
57	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
58	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	5
59	Absent	Absent	Absent	Present	Infiltrating	Mild	Absent	Free with presence of UDH	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
60	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	0	18	Not recovered	Not recovered	0	8	0	26	0	Absent	Not seen	0
61	Present	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	19	Not recovered	Not recovered	Not recovered	Not recovered	0	19	0	Absent	Not seen	0
62	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
63	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	16	20	Not recovered	Not recovered	Not recovered	Not recovered	16	20	3	Absent	Not seen	8
64	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	19	Not recovered	Not recovered	0	8	0	27	0	Absent	Not seen	0
65	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
66	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	0	8	0	3	Not recovered	Not recovered	0	11	0	Absent	Not seen	8
67	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	Three	12	Not recovered	Not recovered	2	9	5	21	3	Present	Not seen	8

S. No.	PR (out of 8)	HER 2/ neu	FISH analysis (in case of equivocal HER 2/ neu)	Ki-67 Percentage of Positive Nuclei	Additional marker E-cadherin	Additional marker EMA	Additional marker CK	Additional marker p63	Additional marker Mammaglobin	Additional marker p40	Additional marker Vimentin	Additional marker SMA	Additional marker 34BE12	Additional marker Synaptophysin	Additional marker Chromogranin A	Additional marker CK 5/6	Additional marker SOX-10	Additional marker GATA-3	Molecular Subtype
47	0	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Absent	Triple Negative
48	5	Negative	Not applicable	10	Lost	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-A
49	0	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Focal strong positive	Absent	Absent	Triple Negative
50	8	Positive	Not applicable	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
51	0	Positive	Not applicable	20	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
52	8	Positive	Positive	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
53	8	Equivocal	Negative	22	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
54	0	Positive	Not applicable	65	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
55	0	Equivocal	Negative	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Triple Negative
56	8	Negative	Not applicable	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
57	0	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse moderate positive	Triple Negative
58	5	Positive	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
59	0	Equivocal	Negative	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Absent	Triple Negative
60	0	Negative	Not applicable	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Diffuse moderate positive	Triple Negative
61	0	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Absent	Triple Negative
62	0	Positive	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
63	8	Negative	Not applicable	50	Lost	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
64	0	Negative	Not applicable	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse moderate positive	Triple Negative
65	8	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
66	8	Equivocal	Negative	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
67	8	Equivocal	Negative	20	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B

S. No.	Patient's name	Age	Sex	MRD no.	Histopathology No.	IHC No.	Presented with breast lump	Presented with breast pain/ heaviness	Presented with nipple enlargement/ discharge/ retraction	Duration of symptoms of presenting illness	Personal history	Past history	Family history	Breast laterality	Breast quadrant	cStage	cT	cN	cM	cGrade	Response to chemotherapy
68	PR	57	F	1439394	14952/22	3/23	Yes	No	No	15 days	Post-menopausal	Not significant	Not significant	Right	Central	IIIA	3	1	0	3	Not applicable
69	KR	71	F	1357562	14957/22	9/23;1585/22	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Right	Upper inner	IB	2	0	0	2	Not applicable
70	D	54	F	1436726	14770/22	16/23	Yes	No	No	3-4 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
71	PC	49	F	1281103	13574/22	18/23	Yes	No	No	6 months	Peri-menopausal	Not significant	Not significant	Bilateral	Left: Upper (outer, inner) and lower	Not known	Not known	Not known	Not known	Not known	Not applicable
72	PB	61	F	1441263	101/23	19/23	Yes	No	No	Not known	Not known	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
73	JK	62	F	1437735	14842/22	32/23	Yes	No	No	7 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
74	KK	66	F	1441653	205/23	42/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
75	RK	42	F	1341837	14805/22	43/23	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
76	KD	55	F	1219794	7865/22	52/23	Yes	No	No	2.5 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Present
77	RJ	52	F	1438924	69/23	58/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Lower outer	IB; T1c pN0M0; G2	1c	0	0	2	Not applicable
78	SK	54	F	1437273	336/23	64/23	Yes	No	No	3 months	Peri-menopausal; AmenorrheaX1.5 months; Parity:2; Last child birth: 23 years ago; Lactational history: Present; Intake of OCPs: Absent	Not significant	Not significant	Left	Upper outer	III	2	0	0	Not known	Not applicable
79	PK	36	F	1443790	454/23	72/23	Yes	No	No	15 days	Pre-menopausal	Not significant	Not significant	Left	Lower	IIIA	1c	2a	0	2	Not applicable
80	SK	58	F	1447759	566/23	80/23	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Left	Not known	X	2	3	0	3	Not applicable

S. No.	Mammography/ USG BIRADS	Evidence of metastasis in CT scan	PET scan findings/ LN metastasis	Pleural Fluid	FNAC (if any)	Types of specimens	Status of overlying skin	Nipple retracted	Growth	No. of lesions	Size of growth	Distance from overlying skin (in cms)	Histopathological type	MBR grade	T	Grade of DCIS	Percentage of tumor area	Papillary Pattern DCIS	Micropapillary pattern DCIS	Solid pattern DCIS	Comedo pattern DCIS	Cribriform pattern DCIS	LCIS
68	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
69	V	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.2X2X1.2 cms	2	IDC, NOS	II	2	Intermediate	5	Absent	Absent	Absent	Present	Absent	Absent
70	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Metaplastic carcinoma	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
71	Not known	Not known	FDG avid enhancing mass lesion in upper outer and oinner quadrant of L breast, with multiple FDG avid lesions seen in the lower quadrant. FDG enlarged LNS are seen in the L axillary region. FDG avid enlarged LN seen in the R axilla	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	8.5X5.5X4 cms; 7X4.5X4.2 cms	1.5	IDC, NOS	II	3	Intermediate	30	Absent	Present	Present	Absent	Present	Absent
72	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
73	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Cystic cavity present	Solitary	9.5X7X4.5 cms	0.7	Encapsulated papillary carcinoma	II	3	Intermediate	10	Absent	Absent	Absent	Absent	Absent	Absent
74	IVb	Not known	Not known	Not known	Not known	Total mastectomy without axillary dissection	Normal	No	Present	Solitary	3X2.5X1.5 cms	2	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
75	V	No evidence	Not known	Not known	Benign breast disease (category II Yokohama)	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
76	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Ulcerated (nipple-areola)	No	Present	Solitary	8X5X3.5 cms	1	IDC, NOS	III	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
77	Not known	No evidence	Post-surgical seroma left chest wall region with associated inflammmatory changes. No other abnormal FDG avid lesion seen in rest of the body region.	Not known	Not known	Lumpectomy/ Excision	Normal	Not applicable	Present	Solitary	1.2X1X0.6 cms	Not known	IDC, NOS	II	1	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
78	IV	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.5X2.5X2.0 cms	1.5	IDC, NOS	I	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
79	IV	No evidence	Not known	Not known	Not known	Breast Conservation Surgery (BCS)	Normal	Not applicable	Present	Solitary	2X2X1 cms	Not known	IDC, NOS	II	1	High	60	Absent	Absent	Present	Present	Present	Absent
80	IV	No evidence	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

S. No.	Tumor necrosis	Skin invasion	Lymphovascular invasion	Microcalcifications	Tumor margins	Lymphocytic response at the advancing margins	Perineural invasion	Deep resected margin	Skeletal muscle involvement	Regional lymph nodes positive for metastasis	Total no. of regional lymph nodes	Sentinel lymph nodes positive for metastasis	Total no. of sentinel lymph nodes	Level 3 lymph nodes positive for metastasis	Total no. of level 3 lymph nodes	Total no. of positive lymph nodes	Total no. of lymph nodes examined	N	Extranodal Extension	Treatment induced changes in breast	ER (out of 8)
68	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
69	Absent	Absent	Absent	Present	Infiltrating	Mild	Absent	Free	Absent	Not recovered	Not recovered	0	6	Not recovered	Not recovered	0	6	0	Absent	Not seen	3
70	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
71	Absent	Absent	Present	Present	Infiltrating	Moderate	Absent	Free	Absent	10	18	Not recovered	Not recovered	1	2	11	20	1	Present	Not seen	8
72	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
73	Present	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	19	Not recovered	Not recovered	Not recovered	Not recovered	0	19	0	Absent	Not seen	8
74	Absent	Absent	Absent	Absent	Infiltrating	Marked	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
75	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
76	Present	Absent	Present	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	10	Not recovered	Not recovered	Not recovered	Not recovered	0	10	0	Absent	Present (Haemorrhage, necrosis, sclerosis with foamy macrophages)	0
77	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
78	Present	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	Three	12	2	7	0	5	5	35	2	Present	Not seen	8
79	Absent	Absent	Present	Absent	Infiltrating	Mild	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Present	Not seen	7
80	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	7

S. No.	PR (out of 8)	HER 2/ neu	FISH analysis (in case of equivocal HER 2/ neu)	Ki-67 Percentage of Positive Nuclei	Additional marker E-cadherin	Additional marker EMA	Additional marker CK	Additional marker p63	Additional marker Mammaglobin	Additional marker p40	Additional marker Vimentin	Additional marker SMA	Additional marker 34BE12	Additional marker Synaptophysin	Additional marker Chromogranin A	Additional marker CK 5/6	Additional marker SOX-10	Additional marker GATA-3	Molecular Subtype
68	6	Negative	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
69	0	Positive	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
70	0	Negative	Not applicable	50	Absent	Negative	Focal positive	Focal positive	Absent	Negative	Diffuse positive	Negative	Focal positive	Absent	Absent	Focal strong positive	Absent	Diffuse strong positive	Triple Negative
71	5	Equivocal	Positive	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
72	8	Positive	Not applicable	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
73	8	Negative	Not applicable	Absent	Absent	Absent	Absent	Negative in papillary fronds and periphery of lesion	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
74	5	Negative	Not applicable	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
75	4	Negative	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
76	0	Negative	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Focal weak positive	Absent	Triple Negative
77	2	Negative	Not applicable	95	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Diffuse moderate positive	Triple Negative
78	8	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
79	0	Negative	Not applicable	20	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
80	4	Negative	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B

S. No.	Patient's name	Age	Sex	MRD no.	Histopathology No.	IHC No.	Presented with breast lump	Presented with breast pain/ heaviness	Presented with nipple enlargement/ discharge/ retraction	Duration of symptoms of presenting illness	Personal history	Past history	Family history	Breast laterality	Breast quadrant	cStage	cT	cN	cM	cGrade	Response to chemotherapy
81	SA	72	F	1449791	718/23	100/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Right	Not known	IIIB	4c	1	0	2	Not applicable
82	S	50	F	1450356	789/23	108/23	Yes	No	No	3 months	Post-menopausal; Parity: 3; Last child birth: 28 years ago; Lactational history: Present; Intake of OCPs: Absent	Not significant	Not significant	Left	Upper outer	Not known	Not known	Not known	Not known	Not known	Not applicable
83	VG	52	F	1450474	799/23	109/23	Yes	No	No	1 month	Pre-menopausal; Parity:2; Last child birth: 31 years; Lactational history: Present; Intake of OCPs: Absent	Not significant	Not significant	Left	Lower outer	Not known	2	0	0	X	Not applicable
84	GK	42	F	1448931	759/23	107/23	Yes	No	No	20 days	Post-menopausal	Not significant	Not significant	Left	Lower inner	Not known	Not known	Not known	Not known	Not known	Not applicable
85	SR	37	F	1447026	594/23	115/23	Yes	No	No	Not known	Not known	Not significant	Not significant	Right	Central	IA	1c	0	0	3	Not applicable
86	BK	40	F	1454837	1025/23	122/23	Yes	No	No	2.5 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
87	K	55	F	1440821	1083/23	133/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Lower outer	Not known	Not known	Not known	Not known	Not known	Not applicable
88	KR	60	F	1452004	1066/23	138/23	Yes	No	No	7-10 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
89	PK	37	F	1441275	1204/23	139/23	Yes	No	No	10 days	Menses: Regular in flow and duration; Parity:1	Not significant	Not significant	Left	Retroareolar	Not known	Not known	Not known	Not known	Not known	Not applicable
90	PS	63	F	1455476	1191/23	144/23	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
91	AA	40	F	1460990	1439/23	154/23	Yes	No	No	1.5 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
92	AK	50	F	1408186	1725/23	178/23	Yes	No	No	12-15 days	Post-menopausal	Not significant	Not significant	Right	Upper outer	IIIB	2	3a	0	2	Not applicable
93	AK	65	F	1467215	1920/23	187/23	Yes	No	No	4 months	Post-menopausal	Not significant	Not significant	Left	Upper	Not known	Not known	Not known	Not known	Not known	Not applicable
94	SK	72	F	1473071	2721/23	235/23	Yes	No	No	2 months	Post-menopausal; Parity: 3; Last child birth: 42 years ago; Lactational history: Present; Intake of OCPs: Absent	Not significant	Not significant	Right	Central	IIIA	2	3	0	2	Not applicable
95	BK	59	F	1476845	2611/23	256/23	Yes	No	No	10 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
96	JK	73	F	147486	2540/23	258/23	Yes	No	No	2.5 months	Post-menopausal	Not significant	Not significant	Left	Upper outer	IA	1c	0	0	1	Not applicable
97	S	72	F	1139834	1921/23	264/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Upper outer	IIA	2	0	0	2	Not applicable
98	AK	72	F	1472008	2446/23	274/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Right	Lower outer	Not known	Not known	Not known	Not known	Not known	Not applicable
99	RK	48	F	1481898	2853/23	286/23	Yes	No	No	Not known	Not known	Not known	Not known	Right	Not known	IA	1c	1mi	0	2	Not applicable
100	ND	71	F	1467358	1882/23	292/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Upper outer	IA	2	0	0	2	Not applicable
101	RK	76	F	47477	2994/23	296/23	Yes	No	No	20 days	Post-menopausal	Not significant	Not significant	Right	Not known	IIIA	2	2	0	3	Not applicable

S. No.	Mammography/ USG BIRADS	Evidence of metastasis in CT scan	PET scan findings/ LN metastasis	Pleural Fluid	FNAC (if any)	Types of specimens	Status of overlying skin	Nipple retracted	Growth	No. of lesions	Size of growth	Distance from overlying skin (in cms)	Histopathological type	MBR grade	T	Grade of DCIS	Percentage of tumor area	Papillary Pattern DCIS	Micropapillary pattern DCIS	Solid pattern DCIS	Comedo pattern DCIS	Cribriform pattern DCIS	LCIS
81	Not known	Not known	FDG avid smoothly marginated peripherally enhancing centrally necrotic mass lesion upper and lower quadrants of R breast. FDG avid R axillary LN show partial metabolic resolution. Lung nodules and mediastinal/ hilar lymph nodes show no significant interval	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Mucinous carcinoma	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
82	IVa	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3X2.5X2.2 cms	1	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
83	Not known	Not known	Not known	Not known	Carcinoma (category V Yokohama)	Total mastectomy without axillary dissection	Normal	No	Present	Solitary	3.2X2.2X2.0 cms	1.2	Mucinous carcinoma	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
84	III	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3X2.5X2 cms	2.5	Mucinous carcinoma	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
85	IV	Not known	Not known	Not known	Not known	Total mastectomy without axillary dissection	Normal	No	Present	Solitary	2X2X1.8 cms	1.2	IDC, NOS	III	1	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
86	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
87	V	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	1.6X1X0.6 cms	3.5	IDC, NOS	II	1	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
88	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
89	Not known	No evidence	FDG avid subcentric L ALN- may be inflammatory but metastatic nature is not completely ruled out	Not known	Not known	Lumpectomy/ Excision	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
90	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.2X2.1X1.5 cms	4	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
91	Not known	Not known	Not known	Not known	Not known	Breast Conservation Surgery (BCS)	Normal	Not applicable	Present	Solitary	3X2X1 cms	1	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
92	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.2X2.2X2 cms	1	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
93	V	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
94	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	Not known	Not known	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
95	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Invasive Lobular carcinoma	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
96	IVc	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	1.8X1.4X1 cms	2.2	IDC, NOS	I	1	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
97	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.4X4.1X3.6 cms	2.6	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
98	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4X3.2X3 cms	1.6	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
99	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	II	1	Intermediate	5-10	Absent	Absent	Absent	Present	Present	Absent
100	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	Not known	Not known	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
101	V	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3X2.2X1.5 cms	0.5	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

S. No.	Tumor necrosis	Skin invasion	Lymphovascular invasion	Microcalcifications	Tumor margins	Lymphocytic response at the advancing margins	Perineural invasion	Deep resected margin	Skeletal muscle involvement	Regional lymph nodes positive for metastasis	Total no. of regional lymph nodes	Sentinel lymph nodes positive for metastasis	Total no. of sentinel lymph nodes	Level 3 lymph nodes positive for metastasis	Total no. of level 3 lymph nodes	Total no. of positive lymph nodes	Total no. of lymph nodes examined	N	Extranodal Extension	Treatment induced changes in breast	ER (out of 8)
81	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
82	Absent	Absent	Present	Absent	Pushing with focally infiltrating	Marked	Present	Free	Absent	3	9	Not recovered	Not recovered	0	12	3	21	1	Absent	Not seen	6
83	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
84	Present	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Absent	0	4	0	3	Not recovered	Not recovered	0	7	0	Absent	Not seen	8
85	Present	Absent	Absent	Absent	Infiltrating	Marked	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
86	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
87	Present	Absent	Absent	Absent	Infiltrating	Moderate	Absent	Free	Absent	0	14	Not recovered	Not recovered	0	3	0	17	0	Absent	Not seen	0
88	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	5	18	Not recovered	Not recovered	0	7	5	25	2	Absent	Not seen	4
89	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
90	Present	Absent	Present	Absent	Infiltrating	Mild	Absent	Free	Absent	6	12	Not recovered	Not recovered	7	8	14	20	3	Present	Not seen	0
91	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
92	Present	Absent	Present	Absent	Infiltrating	Mild	Absent	Free	Absent	10	15	Not recovered	Not recovered	6	7	16	22	3	Present	Not seen	0
93	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
94	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Absent	9	15	3	3	2	6	14	24	3	Absent	Not seen	8
95	Absent	Absent	Absent	Absent	Infiltrating	Moderate	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
96	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	8	Not recovered	Not recovered	0	5	0	13	0	Absent	Not seen	8
97	Present	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	17	Not recovered	Not recovered	0	6	0	23	0	Absent	Not seen	0
98	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	18	Not recovered	Not recovered	Not recovered	Not recovered	0	18	0	Absent	Not seen	0
99	Absent	Absent	Present	Present	Infiltrating	No significant response	Absent	Free	Not seen	2	18	Not recovered	Not recovered	Not recovered	Not recovered	2	18	1	Absent	Not seen	8
100	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	0	9	Not recovered	Not recovered	0	14	0	23	0	Absent	Not seen	8
101	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	3	13	Not recovered	Not recovered	4	9	7	22	2	Present	Not seen	8

S. No.	PR (out of 8)	HER 2/ neu	FISH analysis (in case of equivocal HER 2/ neu)	Ki-67 Percentage of Positive Nuclei	Additional marker E-cadherin	Additional marker EMA	Additional marker CK	Additional marker p63	Additional marker Mammaglobin	Additional marker p40	Additional marker Vimentin	Additional marker SMA	Additional marker 34BE12	Additional marker Synaptophysin	Additional marker Chromogranin A	Additional marker CK 5/6	Additional marker SOX-10	Additional marker GATA-3	Molecular Subtype
81	8	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Negative	Negative	Absent	Absent	Positive	Luminal-B
82	0	Negative	Not applicable	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
83	8	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
84	8	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
85	0	Positive	Not applicable	85	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
86	0	Equivocal	Positive	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
87	0	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Absent	Triple Negative
88	0	Positive	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
89	0	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse moderate positive	Diffuse moderate positive	Triple Negative
90	0	Negative	Not applicable	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Absent	Triple Negative
91	8	Equivocal	Negative	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
92	0	Positive	Not applicable	65	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
93	0	Positive	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
94	8	Positive	Not applicable	35	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
95	8	Negative	Not applicable	14	Lost	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-A
96	8	Equivocal	Negative	12	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-A
97	0	Negative	Not applicable	85	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Focal moderate positive	Diffuse moderate positive	Triple Negative
98	0	Negative	Not applicable	95	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Triple Negative
99	8	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
100	4	Negative	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
101	8	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B

S. No.	Patient's name	Age	Sex	MRD no.	Histopathology No.	IHC No.	Presented with breast lump	Presented with breast pain/ heaviness	Presented with nipple enlargement/ discharge/ retraction	Duration of symptoms of presenting illness	Personal history	Past history	Family history	Breast laterality	Breast quadrant	cStage	cT	cN	cM	cGrade	Response to chemotherapy
102	VR	36	F	1486568	3180/23	299/23	Yes	No	No	Not known	Not known	Not known	Not known	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
103	JK	47	F	1481122	2868/23	309/23	Yes	No	No	3 months	Post-menopausal	Not significant	Not significant	Left	Not known	IIA	2	0	0	3	Not applicable
104	RG	38	F	1486229	3324/23	325/23	Yes	No	No	15 days	Menses: Regular in flow and duration; Parity:2; Last child birth: 13 years; Lactational history: Present; Intake of OCPs: Absent	Not significant	Not significant	Right	Upper outer	IB	2	1a	0	2	Not applicable
105	BK	70	F	1481835	3350/23	326/23	Yes	No	No	10 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
106	NK	58	F	1486084	3406/23	327/23	Yes	No	No	1 year	Post-menopausal; Parity: 3; Last child birth: 30 years ago; Lactational history: Present; Intake of OCPs: Absent	Not significant	Not significant	Left	Upper outer	X	2	2	0	X	Not applicable
107	HK	72	F	1488339	3630/23	340/23	Yes	No	No	7 days	Post-menopausal	Not significant	Not significant	Left	Lower and upper outer	IV	2	1	1	2	Not applicable
108	RM	28	F	1493822	3764/23	356/23	Yes	No	No	Not known	Not known	Not known	Not known	Right	Upper outer	IIIB	4d	1	0	Not known	Not applicable
109	BK	65	F	1491381	3677/23	387/23	Yes	No	No	10 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
110	KK	65	F	1495241	H-1829-23	392/23	Yes	No	No	20 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
111	BK	73	F	1491531	3813/23	394/23	Yes	No	No	3 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
112	DK	60	F	1492016	3863/23	397/23	Yes	No	No	12-15 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
113	HK	80	F	1491165	3912/23	402/23	Yes	No	No	2.5 months	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
114	MR	54	F	1496573	4097/23	421/23	Yes	No	No	3 months	Post-menopausal since 2 years; Parity: 3; Last child birth: 23 years ago; Lactational history: Present; Intake of OCPs: Absent	H/o Poliomyelitis present	Not significant	Right	Upper outer	IB	1c	0	0	Not known	Not applicable
115	JK	62	F	1498447	4496/23	433/23	Yes	No	No	12 days	Post-menopausal	Not significant	Not significant	Left	Upper outer	IV	2	2	1	3	Not applicable
116	JK	66	F	1498711	4281/23	503/23	Yes	No	No	1.5-2 months	Post-menopausal; Parity: 2; Last child birth: 40 years ago; Lactational history: Present; Intake of OCPs: Absent	Not significant	Not significant	Left	Not known	IIA	2	0	0	3	Not applicable
117	S	60	F	1500300	4533/23	445/23	Yes	No	No	15 days	Post-menopausal since 6 years; Parity: 2; Last child birth: 30 years ago; Lactational history: Present; Intake of OCPs: Present	Not significant	Not significant	Right	Upper outer	IIA	2	0	0	2	Not applicable
118	SK	52	F	1263081	4592/23	453/23	Yes	No	No	1 month	Post-menopausal; Parity: 2; Last child birth: 34 years ago; Lactational history: Present; Intake of OCPs: Absent	H/o HIV present	Not significant	Right	Upper outer	Not known	Not known	Not known	Not known	Not known	Not applicable

S. No.	Mammography/ USG BIRADS	Evidence of metastasis in CT scan	PET scan findings/ LN metastasis	Pleural Fluid	FNAC (if any)	Types of specimens	Status of overlying skin	Nipple retracted	Growth	No. of lesions	Size of growth	Distance from overlying skin (in cms)	Histopathological type	MBR grade	T	Grade of DCIS	Percentage of tumor area	Papillary Pattern DCIS	Micropapillary pattern DCIS	Solid pattern DCIS	Comedo pattern DCIS	Cribriform pattern DCIS	LCIS
102	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	II	4	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
103	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Absent	Solitary	4X3.5X2 cms	1.5	IDC, NOS	III	2	High	10	Absent	Absent	Present	Present	Absent	Absent
104	IV	Multiple bilateral subcentimetric axillary LNs, Pretracheal LNs	Not known	Not known	Not known	Breast Conservation Surgery (BCS)	Normal	No	Present	Solitary	2.2X1.5X1.0 cms	4	IDC, NOS	II	2	High	40	Absent	Absent	Present	Present	Present	Absent
105	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4X2X2 cms	1.8	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
106	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.5X3X3 cms	1	Invasive papillary carcinoma	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
107	Not known	Abnormal signal intensitiesin the lumbo-sacral vertebrae with compression of L3 and L4	FDG avid mass lesion in the lower and upper-outer quadrant of left breast, low grade FDG avid lymph node in the left axilla. Multiple FDG avid lytic lesions involving cervico-dorso-lumbar vertebrae, multiple ribs, humerus, stnum, scapulae, sacrum, B/L proximal femurii	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
108	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
109	V	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
110	Not known	Not known	Not known	Not known	Not known	Trucut	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
111	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	5.5X2.5X0.5 cms	1	IDC, NOS	II	3	High	10	Absent	Absent	Present	Present	Absent	Absent
112	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.5X1.8X1.5 cms	1.5	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
113	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	1.8X1.4X1 cms	0.5	IDC, NOS	II	1	High	20	Absent	Absent	Present	Absent	Present	Absent
114	III	Not known	Not known	Not known	Not known	Breast Conservation Surgery (BCS)	Not applicable	Not applicable	Present	Solitary	1.5X1.5X0.6 cms	1.8	IDC, NOS	III	1	High	15	Absent	Absent	Present	Present	Present	Absent
115	Not known	Multiple random nodules in B/l lungs-likely metastasis	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
116	Not known	Few subcentimetric nodules seen in b/l lungs-?Metastasis	Post surgical seroma; Low grade FDG avid b/l lung nodules-suspicious metastatic regions	Not known	Not known	Total mastectomy+Axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
117	Not known	Post-operative changes in R anterior chest wall with seroma formation	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4X3.5X3.2 cms	2.5	IDC, NOS	II	2	Intermediate	10	Absent	Absent	Absent	Present	Absent	Absent
118	IV	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	5X4X4 cms	0.5	IDC, NOS	III	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

S. No.	Tumor necrosis	Skin invasion	Lymphovascular invasion	Microcalcifications	Tumor margins	Lymphocytic response at the advancing margins	Perineural invasion	Deep resected margin	Skeletal muscle involvement	Regional lymph nodes positive for metastasis	Total no. of regional lymph nodes	Sentinel lymph nodes positive for metastasis	Total no. of sentinel lymph nodes	Level 3 lymph nodes positive for metastasis	Total no. of level 3 lymph nodes	Total no. of positive lymph nodes	Total no. of lymph nodes examined	N	Extranodal Extension	Treatment induced changes in breast	ER (out of 8)
102	Absent	Ulceration of the overlying skin	Present	Absent	Infiltrating	No significant response	Absent	Free	Absent	19	20	Not recovered	Not recovered	Not recovered	Not recovered	19	20	3	Present	Not seen	8
103	Present	Absent	Absent	Absent	Infiltrating	Moderate	Absent	Free	Absent	0	16	Not recovered	Not recovered	Not recovered	Not recovered	0	16	0	Absent	Not seen	0
104	Absent	Absent	Present	Present	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Present	Not seen	8
105	Absent	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Absent	1	17	Not recovered	Not recovered	0	11	1	28	1	Absent	Not seen	8
106	Absent	Absent	Present	Absent	Infiltrating	No significant response	Absent	Free	Absent	7	15	Not recovered	Not recovered	0	4	7	19	2	Present	Not seen	8
107	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
108	Present	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
109	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	8	13	Not recovered	Not recovered	0	2	8	15	2	Absent	Not seen	8
110	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
111	Absent	Absent	Present	Absent	Infiltrating	No significant response	Absent	Free	Absent	6	12	Not recovered	Not recovered	4	6	10	18	3	Present	Not seen	0
112	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	16	Not recovered	Not recovered	0	1	0	17	0	Absent	Not seen	0
113	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	17	Not recovered	Not recovered	0	4	0	21	0	Absent	Not seen	8
114	Absent	Absent	Present	Absent	Pushing	No significant response	Absent	Free	Not seen	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
115	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
116	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	0	19	Not recovered	Not recovered	0	7	0	26	0	Absent	Not seen	0
117	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Not seen	0	19	Not recovered	Not recovered	0	13	0	32	0	Absent	Not seen	0
118	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	14	Not recovered	Not recovered	4	19	4	33	3	Present	Not seen	0

S. No.	PR (out of 8)	HER 2/ neu	FISH analysis (in case of equivocal HER 2/ neu)	Ki-67 Percentage of Positive Nuclei	Additional marker E-cadherin	Additional marker EMA	Additional marker CK	Additional marker p63	Additional marker Mammaglobin	Additional marker p40	Additional marker Vimentin	Additional marker SMA	Additional marker 34BE12	Additional marker Synaptophysin	Additional marker Chromogranin A	Additional marker CK 5/6	Additional marker SOX-10	Additional marker GATA-3	Molecular Subtype
102	8	Positive	Not applicable	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
103	0	Positive	Not applicable	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	HER 2/ neu enriched
104	8	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
105	8	Negative	Not applicable	13	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-A
106	8	Negative	Not applicable	12	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-A
107	3	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
108	0	Positive	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	HER 2/ neu enriched
109	4	Equivocal	Negative	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
110	8	Negative	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
111	0	Equivocal	Negative	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Absent	Triple Negative
112	0	Equivocal	Negative	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Triple Negative
113	5	Negative	Not applicable	20	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
114	0	Negative	Not applicable	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Triple Negative
115	8	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
116	0	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse moderate positive	Triple Negative
117	0	Positive	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
118	0	Equivocal	Negative	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse moderate positive	Diffuse strong positive	Triple Negative

S. No.	Patient's name	Age	Sex	MRD no.	Histopathology No.	IHC No.	Presented with breast lump	Presented with breast pain/ heaviness	Presented with nipple enlargement/ discharge/ retraction	Duration of symptoms of presenting illness	Personal history	Past history	Family history	Breast laterality	Breast quadrant	cStage	cT	cN	cM	cGrade	Response to chemotherapy
119	MK	53	F	1502357	4660/23	546/23	Yes	No	No	4-5 months	Post-menopausal; Parity: 3; Last child birth: 26 years ago; Lactational history: Present; Intake of OCPs: Absent	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
120	JK	63	F	1495803	4581/23	455/23	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Right	Lower outer	IA	2	0	0	2	Not applicable
121	RK	47	F	1507374	4768/23	456/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
122	VK	50	F	1499596	4218/23	462/23	Yes	No	No	10 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
123	RK	76	F	1504289	4766/23	474/23	Yes	No	No	7 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
124	AK	68	F	1501769	4713/23	476/23	Yes	No	No	2.5 months	Post-menopausal	Not significant	Not significant	Left	Upper outer	IA	1c	0	0	1	Not applicable
125	K	47	F	1499951	4376/23	481/23	Yes	No	No	Not known	Not known	Not known	Not known	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
126	HK	39	F	1506789	4863/23	489/23	Yes	No	No	7 days	Menstrual history: Unremarkable; Parity: 1; Last child birth: 9 years ago; H/o breastfedding: Present; Intake of OCPs: Absent	Not significant	Not significant	Left	Not known	IIIA	2	3	0	2	Not applicable
127	GD	36	F	1501275	4279/23	490/23	Yes	No	No	Not known	Not known	Not known	Not known	Left	Central	IIIB	4b	1a	0	2	Not applicable
128	RK	77	F	1503883	4918/23	493/23	Yes	No	No	10 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
129	AK	75	F	1037074	4916/23	494/23	Yes	No	No	20 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
130	JK	66	F	1498711	O/S Blocks 102A, B, 103A/ 23	503/23	Yes	No	No	4 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
131	US	52	F	1504648	4690/23	508/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Upper outer	IA	2	0	0	2	Not applicable
132	KR	53	F	1513422	5226/23	513/23	Yes	No	No	7 days	Post-menopausal	Not significant	Not significant	Left	Upper outer	IV	4c	X	1	2	Not applicable
133	NB	41	F	1511851	5202/23	518/23	Yes	No	No	6-8 months	Post menopausal (post TAH 3 years ago for uterine fibroid); Parity: 3; Last child birth: 18 years ago; H/o breastfeeding: Present; Intake of OCPs: Absent	Not significant	Not significant	Right	Upper inner	X	3	1	0	Not known	Not applicable
134	HK	36	F	1510646	5188/23	531/23	Yes	No	No	Not known	Not known	Not known	Not known	Left	Upper outer	IIA	2	0	0	3	Not applicable
135	KK	64	F	1510645	5356/23	532/23	Yes	No	No	3-4 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
136	SM	47	F	1515948	5409/23	533/23	Yes	No	No	Not known	Not known	Not known	Not known	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
137	MK	53	F	1502357	4660/23	546/23	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Left	Not known	IIB	2	2a	0	3	Not applicable
138	PK	56	F	295963	4851/23	550/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Right	Upper outer	IIA	2	0	0	3	Not applicable
139	SV	43	F	1516009	5613/23	556/23	Yes	No	No	2-3 months	Pre-menopausal	Not significant	H/o Ca breast in maternal aunt	Right	Lower inner	IIA	2	0	0	2	Not applicable

S. No.	Mammography/ USG BIRADS	Evidence of metastasis in CT scan	PET scan findings/ LN metastasis	Pleural Fluid	FNAC (if any)	Types of specimens	Status of overlying skin	Nipple retracted	Growth	No. of lesions	Size of growth	Distance from overlying skin (in cms)	Histopathological type	MBR grade	T	Grade of DCIS	Percentage of tumor area	Papillary Pattern DCIS	Micropapillary pattern DCIS	Solid pattern DCIS	Comedo pattern DCIS	Cribriform pattern DCIS	LCIS
119	Not known	No evidence	Not known	Not known	Not known	Total mastectomy without axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
120	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.2X1.8X1 cms	1	IDC, NOS	II	2	Intermediate	15	Absent	Absent	Present	Absent	Present	Absent
121	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	I	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
122	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4X3X3 cms	1	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
123	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	1.5X1X1 cms	2	Invasive Lobular carcinoma	II	1	Absent	20	Absent	Absent	Absent	Absent	Absent	Present
124	BIRADS not mentioned	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2X1.5X1.5 cms	1	IDC, NOS	I	1	Intermediate	5	Absent	Absent	Absent	Present	Absent	Absent
125	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2X2X1.5 cms	1.5	Mucinous carcinoma	II	1	High	15	Absent	Absent	Present	Absent	Present	Absent
126	IVC	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.5X4X3 cms	1.5	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
127	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Ulcerated (nipple-areola)	No	Present	Solitary	2X1.5X0.7 cms	0.4	IDC, NOS	II	4	High	10	Absent	Absent	Absent	Present	Absent	Absent
128	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3X3X2.8 cms	2.4	IDC, NOS	III	2	High	20	Absent	Absent	Present	Present	Absent	Absent
129	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.5X3X2.8 cms	1	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
130	Not known	Few subcentimetric nodules seen in b/l lungs- ?Metastasis	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Cystic cavity present (3 cms in diameter)	Solitary	3X2X1.5 cms	1	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
131	BIRADS not mentioned	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3X3X2.4 cms	2	IDC, NOS	II	2	Intermediate	5	Absent	Absent	Absent	Present	Absent	Absent
132	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
133	Not known	Not known	Ill defined infiltrating lesion showing heterogenous enhancement in R breast parenchyma. Soft tissue density lesion noted in upper-inner quadrant of L breast. Cystic lesion noted in L adnexa	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	8X6X4 cms	0.4	IDC, NOS	III	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
134	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.5X3.2X2.6 cms	1	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
135	Not known	Not known	Not known	Not known	Not known	Lumpectomy/ Excision	Not applicable	Not applicable	Not applicable	Not applicable	2.2X1.5X1.2 cms	1	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
136	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Metaplastic carcinoma	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
137	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	5X2X2 cms	2	IDC, NOS	II	2	Intermediate	30	Absent	Absent	Present	Present	Absent	Absent
138	Not known	No evidence	Not known	Not known	Carcinoma (category V Yokohama); R supraclavicular LN: Tuberculosis	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
139	Not known	Not known	FDG avid lesion in L-I quadrant of R breast; no disease elsewhere	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

S. No.	Tumor necrosis	Skin invasion	Lymphovascular invasion	Microcalcifications	Tumor margins	Lymphocytic response at the advancing margins	Perineural invasion	Deep resected margin	Skeletal muscle involvement	Regional lymph nodes positive for metastasis	Total no. of regional lymph nodes	Sentinel lymph nodes positive for metastasis	Total no. of sentinel lymph nodes	Level 3 lymph nodes positive for metastasis	Total no. of level 3 lymph nodes	Total no. of positive lymph nodes	Total no. of lymph nodes examined	N	Extranodal Extension	Treatment induced changes in breast	ER (out of 8)
119	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
120	Absent	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Absent	0	19	Not recovered	Not recovered	0	5	0	24	0	Absent	Not seen	8
121	Absent	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
122	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Not seen	0	15	Not recovered	Not recovered	Not recovered	Not recovered	0	15	0	Absent	Not seen	0
123	Absent	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Absent	0	21	Not recovered	Not recovered	0	4	0	25	0	Absent	Not seen	8
124	Present	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Not seen	0	8	Not recovered	Not recovered	0	3	0	11	0	Absent	Not seen	8
125	Absent	Absent	Absent	Absent	Pushing	No significant response	Absent	Free	Not seen	0	17	Not recovered	Not recovered	Not recovered	Not recovered	0	17	0	Absent	Not seen	8
126	Absent	Absent	Absent	Present	Infiltrating	Mild	Absent	Free	Not seen	14	22	Not recovered	Not recovered	7	8	21	30	3	Present	Not seen	8
127	Absent	Ulceration of the overlying skin	Present	Absent	Infiltrating	No significant response	Absent	Free	Absent	1	21	Not recovered	Not recovered	0	2	1	23	1	Absent	Not seen	0
128	Present	Absent	Absent	Present	Infiltrating	Mild	Absent	Free	Absent	0	15	Not recovered	Not recovered	0	7	0	22	0	Absent	Not seen	0
129	Present	Absent	Absent	Absent	Pushing	No significant response	Absent	Free	Not seen	0	15	Not recovered	Not recovered	0	5	0	20	0	Absent	Not seen	8
130	Present	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	19	Not recovered	Not recovered	0	7	0	26	0	Absent	Not seen	0
131	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Not seen	0	14	Not recovered	Not recovered	Not recovered	Not recovered	0	14	0	Absent	Not seen	8
132	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
133	Absent	Absent	Present	Absent	Infiltrating	Mild	Absent	Free	Not seen	0	8	2	2	0	4	2	14	1	Absent	Not seen	8
134	Absent	Absent	Absent	Absent	Pushing	Mild	Absent	Free	Absent	0	10	Not recovered	Not recovered	0	4	0	14	0	Absent	Not seen	0
135	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Present	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
136	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
137	Absent	Absent	Present	Present	Infiltrating	No significant response	Present	Free	Absent	3	18	3	5	Not recovered	Not recovered	6	23	2	Present	Not seen	8
138	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
139	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0

S. No.	PR (out of 8)	HER 2/ neu	FISH analysis (in case of equivocal HER 2/ neu)	Ki-67 Percentage of Positive Nuclei	Additional marker E-cadherin	Additional marker EMA	Additional marker CK	Additional marker p63	Additional marker Mammaglobin	Additional marker p40	Additional marker Vimentin	Additional marker SMA	Additional marker 34BE12	Additional marker Synaptophysin	Additional marker Chromogranin A	Additional marker CK 5/6	Additional marker SOX-10	Additional marker GATA-3	Molecular Subtype
119	6	Negative	Not applicable	30	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
120	8	Negative	Not applicable	30	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
121	6	Negative	Not applicable	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-A
122	0	Equivocal	Positive	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
123	8	Negative	Not applicable	10	Lost	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-A
124	8	Negative	Not applicable	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
125	8	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
126	8	Negative	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
127	0	Positive	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
128	0	Equivocal	Negative	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Triple Negative
129	0	Negative	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
130	0	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse moderate positive	Triple Negative
131	4	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
132	0	Positive	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	HER 2/ neu enriched
133	8	Negative	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
134	0	Negative	Not applicable	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Diffuse strong positive	Triple Negative
135	8	Negative	Not applicable	60	Absent	Absent	Positive	Absent	Positive	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
136	0	Negative	Not applicable	60	Absent	Absent	Positive in epithelial cells	Absent	Absent	Absent	Positive in spindle cells	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Triple Negative
137	6	Negative	Not applicable	30	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
138	0	Negative	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Focal moderate positive	Absent	Triple Negative
139	0	Positive	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	HER 2/ neu enriched

S. No.	Patient's name	Age	Sex	MRD no.	Histopathology No.	IHC No.	Presented with breast lump	Presented with breast pain/ heaviness	Presented with nipple enlargement/ discharge/ retraction	Duration of symptoms of presenting illness	Personal history	Past history	Family history	Breast laterality	Breast quadrant	cStage	cT	cN	cM	cGrade	Response to chemotherapy
140	DG	61	F	1511325	5550/23	568/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Upper outer	IIA	2	0	0	3	Not applicable
141	SK	56	F	1384461	5682/ 23	574/23	Yes	No	No	10 days	Post-menopausal	Not significant	Not significant	Right	Not known	X	2	0	0	Not known	Not applicable
142	VL	78	F	1516288	5737/ 23	581/23	Yes	No	No	5-6 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
143	VK	53	F	1516955	5758/ 23	582/23	Yes	No	No	3-4 months	Post-menopausal	Not significant	Not significant	Left	Lower outer	IIA	2	0	0	3	Not applicable
144	KR	75	F	1518979	5856/ 23	586/23	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Left	Not known	IV	4b	1	1	2	Not applicable
145	RM	46	F	1521783	5902/23	587/23	Yes	No	No	15 days	Post-menopausal	Not significant	Not significant	Left	Not known	IV	4	2	1	2	Not applicable
146	RB	39	F	1513477	5842/ 23	597/23	Yes	No	No	Not known	Pre-menopausal; Parity:1	Not known	H/o malignancy in maternal uncle	Right	Upper outer	IIIA	2	2	0	2	Not applicable
147	SR	43	F	1519369	5888/ 23	602/23	Yes	No	No	Not known	Not known	Not known	Not known	Left	Upper outer	IIIA	2	3	0	2	Not applicable
148	JK	45	F	1517396	6127/ 23	613/23	Yes	No	No	Not known	Not known	Not known	Not known	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
149	SK	85	F	1526036	6284/ 23	627/23	Yes	No	No	10 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
150	SK	62	F	1513119	6470/ 23	630/23	Yes	No	No	10-15 days	Post-menopausal	Not significant	Not significant	Right	Not known	X	Not known	Not known	Not known	Not known	Not applicable
151	BK	57	F	1517520	6325/23	631/23	Yes	No	No	3 months	Post-menopausal	Not significant	Not significant	Left	Upper inner	IIIA	3	0	0	3	Not applicable
152	SK	45	F	1528545	6515/23	649/23	Yes	No	No	3-4 months	Post-menopausal	Not significant	Not significant	Left	Not known	IIA	2	0	0	3	Not applicable
153	RK	60	F	1528705	6748/23	657/23	Yes	No	No	1 month	Post-menopausal	Not significant	H/o Ca buccal mucosa in father	Left	Upper outer	IA	2	0	0	3	Not applicable
154	KK	51	F	1534518	Absent	658/23	Yes	No	No	3 months	Post-menopausal	Not significant	H/o Ca breast in mother	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
155	SD	56	F	1271667	6872/23	662/23	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Left	Central	IV	4b	3c	1	2	Not applicable
156	SV	35	F	1527383	6454/23	664/23	Yes	No	No	Not known	Not known	Not known	Not known	Right	Outer	Not known	Not known	Not known	Not known	Not known	Not applicable
157	RK	47	F	1530934	6796/23	666/23	Yes	No	Yes	7 days	Post-menopausal; Parity:02; Last child birth: 18 years ago; Lactational history: Present; Intake of OCPs: Absent	Not significant	Not significant	Left	Upper outer	IA	2	0	0	2	Not applicable
158	MR	55	F	1533635	6925/23	669/23	Yes	No	No	15 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
159	TK	42	F	1529951	6877/23	672/23	Yes	No	No	7 days	Menses: Regular in flow and duration; Parity:0; Last child birth: NA; Lactational history: NA ; Intake of OCPs: Absent	Not significant	H/o ?Ca endometrium in mother	Right	Upper outer	X	Not known	Not known	Not known	Not known	Not applicable
160	BK	80	F	1530889	7051/23	673/23	Yes	No	No	10-20 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
161	AK	61	F	1536238	7222/23	685/23	Yes	No	No	2.5 months	Post-menopausal	Not significant	Not significant	Right	Not known	IB	2	2a	0	1	Not applicable
162	RR	72	F	1530627	7335/23	691/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Outer	X	3	1	0	X	Not applicable
163	PM	44	F	1539808	7445/23	692/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable

S. No.	Mammography/ USG BIRADS	Evidence of metastasis in CT scan	PET scan findings/ LN metastasis	Pleural Fluid	FNAC (if any)	Types of specimens	Status of overlying skin	Nipple retracted	Growth	No. of lesions	Size of growth	Distance from overlying skin (in cms)	Histopathological type	MBR grade	T	Grade of DCIS	Percentage of tumor area	Papillary Pattern DCIS	Micropapillary pattern DCIS	Solid pattern DCIS	Comedo pattern DCIS	Cribriform pattern DCIS	LCIS
140	Not known	No evidence	Not known	Not known	Not known	Breast Conservation Surgery (BCS)	Not applicable	Not applicable	Present	Solitary	2.5X2X1.5 cms	4	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
141	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.8X1.5X1.2 cms	1.8	Invasive Lobular carcinoma	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
142	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.2X1.5X1 cms	0.6	Invasive Lobular carcinoma	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
143	Not known	Not known	FDG avid lesion in LO quadrant of L breast	Not known	Not known	Breast Conservation Surgery (BCS)	Not applicable	Not applicable	Present	Solitary	2.5X1.5X1.2 cms	2.2	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
144	Not known	Not known	Not known	Not known	Not known	Lumpectomy/ Excision	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
145	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
146	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.5X3.2X2 cms	4	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
147	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4X3X2.5 cms	1.5	IDC, NOS	II	2	Intermediate	10	Absent	Absent	Absent	Present	Absent	Absent
148	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Not known	Not known	Not known	Not known	Not known	Not known	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
149	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3X2X1.6 cms	3.5	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
150	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
151	IV	Not known	Malignant primary disease; FDG avid enlarged L ALN, low grade FDG avid R lower lung lesion- more likely infective; mild FDG uptake b/l adrenal gland	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	8X7X6 cms	0.5	IDC, NOS	III	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
152	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3X3X2.5 cms	3	IDC, NOS	III	2	Absent	10	Absent	Absent	Present	Present	Present	Absent
153	Not known	Well defined enhancing lesion in segment VII of liver	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.2X1.8X1.5 cms	1	IDC, NOS	III	2	Absent	5	Absent	Absent	Present	Absent	Absent	Absent
154	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
155	V	Multiple target lesions in the liver s/o metastasis; Tiny scattered nodules in B/L lung fields- highly suspicious of metastasis	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
156	VI	Not known	Metastatic R axillary LAP	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	5.4X4X2 cms	1	IDC, NOS	II	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
157	IV	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.6X2.2X2 cms	2.2	IDC, NOS	II	2	Absent	15	Absent	Absent	Absent	Present	Absent	Absent
158	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.3X3.2X3 cms	2.2	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
159	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.2X2.6X2.4 cms	1.5	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
160	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
161	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.4X3.2X2.5 cms	3	IDC, NOS	I	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
162	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	5.4X3.5X2.8 cms	2.8	Invasive Lobular carcinoma	II	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
163	Not known	Not known	Not known	Not known	Not known	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

S. No.	Tumor necrosis	Skin invasion	Lymphovascular invasion	Microcalcifications	Tumor margins	Lymphocytic response at the advancing margins	Perineural invasion	Deep resected margin	Skeletal muscle involvement	Regional lymph nodes positive for metastasis	Total no. of regional lymph nodes	Sentinel lymph nodes positive for metastasis	Total no. of sentinel lymph nodes	Level 3 lymph nodes positive for metastasis	Total no. of level 3 lymph nodes	Total no. of positive lymph nodes	Total no. of lymph nodes examined	N	Extranodal Extension	Treatment induced changes in breast	ER (out of 8)
140	Absent	Absent	Absent	Absent	Infiltrating	Marked	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
141	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Present	Free	Absent	0	17	Not recovered	Not recovered	0	3	0	20	0	Absent	Not seen	8
142	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	13	Not recovered	Not recovered	0	5	0	18	0	Absent	Not seen	8
143	Present	Absent	Absent	Present	Infiltrating	Mild	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	7
144	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
145	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	4
146	Present	Absent	Present	Absent	Infiltrating	Mild	Absent	Free	Absent	0	9	Not recovered	Not recovered	0	6	0	15	2	Present	Not seen	0
147	Absent	Absent	Present	Absent	Infiltrating	Mild	Absent	Free	Not seen	10	14	Not recovered	Not recovered	3	5	13	19	3	Present	Not seen	8
148	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Absent	Not known	0	18	Not recovered	Not recovered	0	2	0	20	0	Absent	Not seen	3
149	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Not seen	0	16	Not recovered	Not recovered	0	8	0	24	0	Absent	Not seen	8
150	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
151	Absent	Absent	Absent	Absent	Infiltrating	Moderate	Absent	Free	Absent	0	21	Not recovered	Not recovered	0	4	0	25	0	Absent	Not seen	0
152	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	23	Not recovered	Not recovered	0	10	0	33	0	Absent	Not seen	0
153	Absent	Absent	Absent	Absent	Infiltrating	Moderate	Absent	Free	Absent	Not recovered	Not recovered	0	6	Not recovered	Not recovered	0	6	0	Absent	Not seen	8
154	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
155	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
156	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Not seen	16	16	Not recovered	Not recovered	Not recovered	Not recovered	16	16	3	Present	Not seen	8
157	Present	Absent	Present	Absent	Infiltrating	Mild	Absent	Free	Absent	0	21	Not recovered	Not recovered	0	3	0	24	0	Absent	Not seen	8
158	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Not seen	0	19	Not recovered	Not recovered	0	4	0	23	0	Absent	Not seen	7
159	Present	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Not seen	0	19	Not recovered	Not recovered	0	11	0	30	0	Absent	Not seen	0
160	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
161	Absent	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Absent	7	15	Not recovered	Not recovered	0	4	7	19	2	Absent	Not seen	8
162	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Present	Free	Not seen	2	23	Not recovered	Not recovered	0	8	2	31	1	Absent	Not seen	8
163	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8

S. No.	PR (out of 8)	HER 2/ neu	FISH analysis (in case of equivocal HER 2/ neu)	Ki-67 Percentage of Positive Nuclei	Additional marker E-cadherin	Additional marker EMA	Additional marker CK	Additional marker p63	Additional marker Mammaglobin	Additional marker p40	Additional marker Vimentin	Additional marker SMA	Additional marker 34BE12	Additional marker Synaptophysin	Additional marker Chromogranin A	Additional marker CK 5/6	Additional marker SOX-10	Additional marker GATA-3	Molecular Subtype
140	0	Negative	Not applicable	75	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Focal strong positive	Absent	Absent	Triple Negative
141	7	Negative	Not applicable	20	Lost	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
142	8	Negative	Not applicable	20	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
143	0	Negative	Not applicable	18	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
144	0	Positive	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
145	2	Positive	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
146	0	Positive	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse moderate positive	HER 2/ neu enriched
147	8	Positive	Not applicable	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
148	0	Positive	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
149	3	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
150	8	Positive	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
151	0	Negative	Not applicable	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Absent	Triple Negative
152	0	Negative	Not applicable	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Triple Negative
153	4	Positive	Not applicable	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
154	0	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Triple Negative
155	0	Positive	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	HER 2/ neu enriched
156	7	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
157	8	Negative	Not applicable	30	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
158	7	Equivocal	Negative	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
159	0	Equivocal	Negative	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse weak positive	Absent	Triple Negative
160	7	Equivocal	Positive	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
161	8	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
162	8	Negative	Not applicable	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
163	7	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B

S. No.	Patient's name	Age	Sex	MRD no.	Histopathology No.	IHC No.	Presented with breast lump	Presented with breast pain/ heaviness	Presented with nipple enlargement/ discharge/ retraction	Duration of symptoms of presenting illness	Personal history	Past history	Family history	Breast laterality	Breast quadrant	cStage	cT	cN	cM	cGrade	Response to chemotherapy
164	KK	51	F	1542097	7477/23	695/23	Yes	No	No	4-5 months	Post-menopausal	Not significant	Not significant	Right	Upper outer	IV	3	3c	1	1	Not applicable
165	NB	67	F	1542016	7600/23	716/23	Yes	No	No	3 months	Post-menopausal	Not significant	Not significant	Right	Upper inner	IB	2	2a	0	2	Not applicable
166	SS	52	F	1534759	7650/23	724/23	Yes	No	No	Not known	Not known	Not known	Not known	Left	Upper outer	IA	2	0	0	1	Not applicable
167	SD	65	F	1542637	7707/23	727/23	Yes	No	No	20 days	Post-menopausal	Not significant	Not significant	Right	Upper outer	IV	3	3	1	2	Not applicable
168	PS	42	F	1541862	7709/23	729/23	Yes	No	No	6 months	Not significant	Not significant	Not significant	Left	Upper outer	IA	2	0	0	2	Not applicable
169	RJ	44	F	1542878	7867/23	741/23	Yes	No	No	15 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
170	RS	41	F	1554230	8613/23	764/23	Yes	No	No	15 days	Not known	Not known	Not significant	Left	Central	Not known	Not known	Not known	Not known	Not known	Not applicable
171	RK	66	F	1554395	8538/23	785/23	Yes	No	No	4-5 months	Post-menopausal	Not significant	Not significant	Left	Upper inner	IB	2	1a	0	2	Not applicable
172	GK	39	F	1555247	8566/23	786/23	Yes	No	No	3-4 months	Pre-menopausal	Not known	Not known	Left	Upper inner	Not known	Not known	Not known	Not known	Not known	Not applicable
173	S	70	F	1555996	8581/23	808/23	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Left	Axillary tail of breast	IV	4a	X	1	2	Not applicable
174	SR	51	F	1556367	8740/23	811/23	Yes	No	No	5 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
175	AV	59	F	1555033	8829/23	812/23	Yes	No	No	3 months	Post-menopausal	Not significant	Not significant	Right	Upper outer	IIA	2	0	0	2	Not applicable
176	RD	88	F	1547143	8973/23	828/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
177	BK	64	F	1563025	9196/23	839/23	Yes	No	No	15 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
178	AR	59	F	1561983	9256/23	845/23	Yes	No	No	3 months	Post-menopausal	Not significant	Not significant	Right	Upper outer	IB	2	2a	0	2	Not applicable
179	AT	68	F	1568802	9532/23	864/23	Yes	No	No	3 months	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
180	NA	43	F	928039	9245/23	889/23	Yes	No	No	5 months	Not known	Not known	Not known	Right	Upper outer	IA	2	0	0	2	Not applicable
181	KK	45	F	1571499	9919/23	899/23	Yes	No	No	Not known	Not known	Not known	Not known	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
182	GK	35	F	1184731	10239/22	903/23	Yes	No	No	Not known	Not known	Not known	Not known	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
183	RS	50	M	1564274	9464/23	904/23	Yes	No	No	15 days	Not applicable	Not applicable	Not applicable	Left	Not known	IIIA	4b	0	0	2	Not applicable
184	SK	47	F	1566216	9428/23	905/23	Yes	No	No	3 months	Post-menopausal	Not significant	Not significant	Right	Upper outer	IB	2	2a	0	2	Not applicable
185	SR	55	F	1574841	10066/23	918/23	Yes	No	No	3-4 weeks	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
186	KK	68	F	1562621	9952/23	920/23	Yes	No	No	2 months	Post-menopausal	Not significant	Not significant	Right	Upper inner	IA	2	0	0	1	Not applicable

S. No.	Mammography/ USG BIRADS	Evidence of metastasis in CT scan	PET scan findings/ LN metastasis	Pleural Fluid	FNAC (if any)	Types of specimens	Status of overlying skin	Nipple retracted	Growth	No. of lesions	Size of growth	Distance from overlying skin (in cms)	Histopathological type	MBR grade	T	Grade of DCIS	Percentage of tumor area	Papillary Pattern DCIS	Micropapillary pattern DCIS	Solid pattern DCIS	Comedo pattern DCIS	Cribriform pattern DCIS	LCIS
164	Not known	B/L lymphangitis carcinomatosis with L moderate pleural effusion and minimal pneumothorax	FDG avid enhancing mass R breast, , multiple lesions L breast show decrease in size, involvong bone and LNS show decrease in size	Atypical cells	Right neck nodule: Metastatic carcinomatous deposits; Posterior neck swelling: Metastatic carcinomatous deposits	Trucut	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	I	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
165	Not known	No evidence	Not known	Not known	Not known	Total mastectomy without axillary dissection	Normal	No	Present	Solitary	4.5X4X3.2 cms	1.6	IDC, NOS	II	3	Absent	<10%	Absent	Absent	Absent	Present	Absent	Absent
166	Not known	Not known	Not known	Not known	Not known	Breast Conservation Surgery (BCS)	Not applicable	Not applicable	Present	Solitary	3.8X3X2 cms	1.5	IDC, NOS	I	2	Absent	5	Absent	Absent	Present	Absent	Absent	Absent
167	Not known	Suggestive of skeletal metastases	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	7X3.5X3 cms	2	IDC, NOS	II	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
168	Not known	Focal metabolic activity in segment II of liver	FDG avid L breast lesion UO quadrant with subcentimetric L axillary LNs. Focal metabolic activity in segment II of liver	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.4X2.2X1.5 cms	1.2	IDC, NOS	II	2	High	20	Absent	Absent	Present	Present	Present	Absent
169	Not known	2 hypodense lesions in segment VII and IVa of liver	Not known	Not known	Not known	Lumpectomy/ Excision	Normal	Not applicable	Present	Solitary	2.8X1.5X1 cms	3	IDC, NOS	I	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
170	Not known	5 mm subsolid nodule in lateral basal segment of R lower lobe	Not known	Not known	Not known	Breast Conservation Surgery (BCS)	Normal	No	Present	Solitary	2X1.6X1 cms	3.8	Cribriform carcinoma	II	1	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
171	Not known	Hypoenhancing lesion in R adrenal	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.5X2X1.2 cms	2	Mucinous carcinoma	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
172	BIRADS not mentioned	Not known	Not known	Not known	Not known	Trucut	Normal	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
173	Not known	Not known	Not known	Not known	Not known	Trucut	Normal	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	II	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
174	VI	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.5X2X1.8 cms	1.8	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
175	V	No evidence	Not known	Not known	Not known	Total mastectomy without axillary dissection	Normal	No	Present	Solitary	2.5X2X1.8 cms	0.8	IDC, NOS	II	2	Absent	10	Absent	Absent	Present	Present	Absent	Absent
176	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	8X7X5.4 cms	Causing ulceration of the overlying skin	IDC, NOS	III	4	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
177	Not known	Not known	Not known	Not known	Not known	Lumpectomy/ Excision	Normal	Not applicable	Present	Solitary	2.8X2.2X1.0 cms	Not known	IDC, NOS	I	2	Absent	25	Absent	Present	Present	Absent	Present	Absent
178	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.2X2.2X1.8 cms	1.8	IDC, NOS	II	2	Intermediate	25	Absent	Absent	Present	Present	Absent	Absent
179	Not known	Not known	Not known	Not known	Not known	Trucut	Normal	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
180	V	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.6X2.8X2.5 cms	1	Invasive Lobular carcinoma	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
181	Not known	No evidence	Not known	Not known	Not known	Lumpectomy/ Excision	Normal	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
182	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Nodules present	No	Present	Solitary	8X7X3 cms	1	IDC, NOS	I	2	Intermediate	15	Absent	Absent	Present	Present	Present	Absent
183	Not known	Not known	Not known	Not known	Not known	Total mastectomy without axillary dissection	Normal	No	Present	Solitary	2.8X1.2X0.8 cms	0.1	IDC, NOS	II	4	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
184	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3.2X2.5X2.2 cms	1	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
185	Not known	Not known	Not known	Not known	Not known	Trucut	Normal	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	I	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
186	Not known	No evidence	Not known	Not known	Suspicious for malignancy (Category IV Yokohama)	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3X2.8X2.5 cms	1.4	IDC, NOS	I	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

S. No.	Tumor necrosis	Skin invasion	Lymphovascular invasion	Microcalcifications	Tumor margins	Lymphocytic response at the advancing margins	Perineural invasion	Deep resected margin	Skeletal muscle involvement	Regional lymph nodes positive for metastasis	Total no. of regional lymph nodes	Sentinel lymph nodes positive for metastasis	Total no. of sentinel lymph nodes	Level 3 lymph nodes positive for metastasis	Total no. of level 3 lymph nodes	Total no. of positive lymph nodes	Total no. of lymph nodes examined	N	Extranodal Extension	Treatment induced changes in breast	ER (out of 8)
164	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
165	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
166	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
167	Absent	Absent	Present	Absent	Infiltrating	Mild	Absent	Free	Absent	16	19	Not recovered	Not recovered	4	6	20	25	3	Present	Not seen	6
168	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Not seen	0	11	0	5	Not recovered	Not recovered	0	16	0	Absent	Not seen	8
169	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Absent	8
170	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Not seen	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
171	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	0	18	1	18	0	1	1	27	1	Present	Not seen	8
172	Present	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	6
173	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
174	Absent	Absent	Present	Absent	Infiltrating	Mild	Absent	Free	Not seen	1	12	Not recovered	Not recovered	0	5	1	17	1	Absent	Not seen	8
175	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
176	Present	Ulceration of the overlying skin	Present	Absent	Infiltrating	Mild	Present	Free	Absent	10	14	Not recovered	Not recovered	Not recovered	Not recovered	10	14	3	Present	Not seen	8
177	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
178	Present	Absent	Present	Present	Infiltrating	Mild	Absent	Free	Absent	5	18	Not recovered	Not recovered	0	6	0	24	2	Present	Not seen	8
179	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
180	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Not seen	0	21	Not recovered	Not recovered	Not recovered	Not recovered	0	21	0	Absent	Not seen	8
181	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
182	Present	Involvement of dermis	Present	Present	Infiltrating	No significant response	Absent	Free	Absent	6	23	Not recovered	Not recovered	Not recovered	Not recovered	6	23	2	Present	Not seen	0
183	Absent	Ulceration of the overlying skin	Absent	Absent	Infiltrating	No significant response	Present	Free	Not seen	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
184	Absent	Absent	Present	Absent	Infiltrating	No significant response	Absent	Free	Absent	8	21	Not recovered	Not recovered	Not recovered	Not recovered	8	21	2	Present	Not seen	7
185	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	8
186	Absent	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Not seen	0	19	Not recovered	Not recovered	0	4	0	23	0	Absent	Not seen	8

S. No.	PR (out of 8)	HER 2/ neu	FISH analysis (in case of equivocal HER 2/ neu)	Ki-67 Percentage of Positive Nuclei	Additional marker E-cadherin	Additional marker EMA	Additional marker CK	Additional marker p63	Additional marker Mammaglobin	Additional marker p40	Additional marker Vimentin	Additional marker SMA	Additional marker 34BE12	Additional marker Synaptophysin	Additional marker Chromogranin A	Additional marker CK 5/6	Additional marker SOX-10	Additional marker GATA-3	Molecular Subtype
164	8	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
165	8	Positive	Positive	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
166	8	Negative	Not applicable	30	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
167	6	Equivocal	Negative	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
168	8	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
169	8	Equivocal	Not done	20	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
170	3	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
171	8	Negative	Not applicable	20	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
172	3	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
173	6	Negative	Not applicable	40	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
174	0	Equivocal	Negative	75	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
175	0	Negative	Not applicable	65	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Focal strong positive	Diffuse weak positive	Absent	Triple Negative
176	8	Equivocal	Not done	75	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
177	3	Negative	Not applicable	12	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-A
178	3	Positive	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
179	7	Negative	Not applicable	50	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
180	8	Equivocal	Positive	40	Lost	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
181	0	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse moderate positive	Triple Negative
182	0	Positive	Not applicable	60	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
183	8	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
184	8	Equivocal	Negative	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
185	8	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
186	8	Negative	Not applicable	30	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B

S. No.	Patient's name	Age	Sex	MRD no.	Histopathology No.	IHC No.	Presented with breast lump	Presented with breast pain/ heaviness	Presented with nipple enlargement/ discharge/ retraction	Duration of symptoms of presenting illness	Personal history	Past history	Family history	Breast laterality	Breast quadrant	cStage	cT	cN	cM	cGrade	Response to chemotherapy
187	KP	74	F	1567960	10012/23	922/23	Yes	No	No	3 weeks	Post-menopausal	Not significant	Not significant	Left	Upper outer	X	4b	3	0	3	Not applicable
188	AS	49	F	1565697	10068/23	929/23	Yes	No	No	10 days	Post-menopausal	Not significant	Not significant	Left	Upper outer	IIIA	2	1a	0	3	Not applicable
189	BK	44	F	1566027	9448/23	938/23	Yes	No	No	6 months	Not known	Not significant	Not significant	Right	Not known	IA	2	1	0	1	Not applicable
190	HK	58	F	1552474	9352/23	941/23	Yes	No	No	4.5-5 months	Post-menopausal	Not significant	Not significant	Left	Upper inner	IA	2	0	0	1	Not applicable
191	R	42	F	1581526	10591/23	983/23	Yes	No	No	Not known	Not known	Not known	Not known	Left	Not known	IB	2	2a	0	1	Not applicable
192	RR	41	F	1574724	10154/23	975/23	Yes	No	No	Not known	Not known	Not known	Not known	Left	Upper outer	Not known	Not known	Not known	Not known	Not known	Not applicable
193	MJ	50	F	1572195	9981/23	957/23	Yes	No	No	8-10 days	Post-menopausal	Not significant	Not significant	Left	Upper outer	IIIC	1	2	0	3	Not applicable
194	V	48	F	1580409	10547/23	976/23	Yes	No	No	1 month	Post-menopausal	Not significant	Not significant	Left	Upper outer	IIIB	1	2a	0	Not known	Not applicable
195	V	34	F	867281	10544/23	977/23	Yes	No	No	Not known	Not known	Not known	Not known	Left	Lower outer	IA	2	0	0	1	Not applicable
196	PD	66	F	1578316	10543/23	978/23	Yes	No	No	7 days	Post-menopausal	Not significant	H/o Uterine Ca in paternal aunt, Prostate Ca in paternal uncle, Metastatic breast Ca in niece and Brain tumor in nephew	Left	Lower inner	IIA	2	0	0	2	Not applicable
197	A	56	F	1575857	10369/23	982/23	Yes	No	No	15 days	Post-menopausal	Not significant	Not significant	Right	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
198	SS	72	F	1581585	10624/23	993/23	Yes	No	No	Not known	Post-menopausal	Not significant	Not significant	Right	Upper outer	Not known	Not known	Not known	Not known	Not known	Not applicable
199	RS	43	F	268442	10769/23	1002/23	Yes	No	No	Not known	Not known	Not known	Not known	Left	Upper inner	IIIA	3	2a	0	3	Not applicable
200	JK	67	F	312327	10851/23	1005/23	Yes	No	No	1 month	Not significant	Not significant	Not significant	Right	Upper inner	IA	2	0	0	2	Not applicable
201	KR	71	F	465152	9350/23	1008/23	Yes	No	No	20 days	Post-menopausal	Not significant	Not significant	Left	Not known	Not known	Not known	Not known	Not known	Not known	Not applicable
202	SD	54	F	1570658	9848/23	1011/23	Yes	No	No	10-20 days	Post-menopausal	Not significant	Not significant	Left	Upper outer	IIB	3	0	0	3	Not applicable
203	NC	67	F	1570618	10914/23	1012/23	Yes	No	No	7 days	Post-menopausal	Not significant	Not significant	Left	Upper outer	IA	2	0	0	1	Not applicable

S. No.	Mammography/ USG BIRADS	Evidence of metastasis in CT scan	PET scan findings/ LN metastasis	Pleural Fluid	FNAC (if any)	Types of specimens	Status of overlying skin	Nipple retracted	Growth	No. of lesions	Size of growth	Distance from overlying skin (in cms)	Histopathological type	MBR grade	T	Grade of DCIS	Percentage of tumor area	Papillary Pattern DCIS	Micropapillary pattern DCIS	Solid pattern DCIS	Comedo pattern DCIS	Cribriform pattern DCIS	LCIS
187	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	7X6.8X2.5 cms	1	IDC, NOS	III	3	High	30	Absent	Absent	Present	Present	Present	Absent
188	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.3X1.8X1.0 cms	3	IDC, NOS	III	2	Absent	10	Absent	Absent	Absent	Absent	Present	Absent
189	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.8X4X3 cms	2	IDC, NOS	I	2	Absent	10	Absent	Absent	Present	Absent	Absent	Absent
190	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	4.2X3.3X1 cms	1.2	IDC, NOS	I	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
191	Not known	No evidence	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	I	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
192	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.5X2X2 cms	5	IDC, NOS	II	2	High	15	Absent	Absent	Present	Absent	Present	Absent
193	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2X2X1 cms	1.5	IDC, NOS	III	1	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
194	Not known	Not known	Not known	Not known	Not known	Total mastectomy without axillary dissection	Normal	No	Present	Solitary	1.5X1X1 cms	1.5	IDC, NOS	II	1	Absent	15	Absent	Absent	Present	Present	Absent	Absent
195	Not known	No evidence	FDG avid enhancing lesion in LO quadrant of L breast, breast parenchymal thickening	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.8X2X1 cms	1	IDC, NOS	I	2	Absent	10	Absent	Absent	Present	Absent	Absent	Absent
196	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.2X1.3X1.2 cms	1.5	IDC, NOS	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
197	Not known	Not known	Not known	Positive- Carcinoma	Not known	Lumpectomy/ Excision	Normal	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	IDC, NOS	III	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
198	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.5X1X0.8 cms	0.8	Mixed IDC-NOS and invasive lobular carcinoma	III	2	Absent	5-7	Present	Absent	Present	Absent	Present	Absent
199	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	5.1X5X2.5 cms	2	IDC, NOS	III	3	High	25	Absent	Absent	Absent	Present	Absent	Absent
200	IV	Multiple subcentimetric solid and subsolid nodules in both lungs (R>L)- Non specific; Multiple	Not known	Not known	Carcinoma (category V Yokohama)	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	3X2X1.5 cms	3	IDC, NOS	II	2	High	40	Absent	Absent	Present	Present	Present	Absent
201	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	6.5X4.4X4.2 cms	0.3	Solid papillary carcinoma	II	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
202	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	5.8X4.6X4.2 cms	1.8	IDC, NOS	III	3	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
203	Not known	Not known	Not known	Not known	Not known	Total mastectomy+Axillary dissection	Normal	No	Present	Solitary	2.5X2X2 cms	2	Mucinous carcinoma	II	2	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

S. No.	Tumor necrosis	Skin invasion	Lymphovascular invasion	Microcalcifications	Tumor margins	Lymphocytic response at the advancing margins	Perineural invasion	Deep resected margin	Skeletal muscle involvement	Regional lymph nodes positive for metastasis	Total no. of regional lymph nodes	Sentinel lymph nodes positive for metastasis	Total no. of sentinel lymph nodes	Level 3 lymph nodes positive for metastasis	Total no. of level 3 lymph nodes	Total no. of positive lymph nodes	Total no. of lymph nodes examined	N	Extranodal Extension	Treatment induced changes in breast	ER (out of 8)
187	Present	Involvement of dermis	Present	Present	Infiltrating	No significant response	Absent	Free	Not seen	19	20	Not recovered	Not recovered	0	5	19	25	3	Present	Not seen	8
188	Present	Absent	Present	Absent	Infiltrating	Mild	Present	Free	Not seen	1	24	Not recovered	Not recovered	0	3	1	27	1	Absent	Not seen	0
189	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Not seen	1	14	Not recovered	Not recovered	Not recovered	Not recovered	1	14	1	Absent	Not seen	8
190	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Not seen	0	14	Not recovered	Not recovered	Not recovered	Not recovered	0	14	0	Absent	Not seen	8
191	Absent	Absent	Absent	Present	Infiltrating	Mild	Absent	Free	Absent	7	18	Not recovered	Not recovered	Not recovered	Not recovered	7	18	2	Absent	Not seen	8
192	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Not seen	1	20	Not recovered	Not recovered	Not recovered	Not recovered	1	20	1	Present	Not seen	7
193	Absent	Absent	Absent	Absent	Infiltrating	Marked	Absent	Free	Absent	6	31	Not recovered	Not recovered	0	3	Six	34	2	Present	Not seen	0
194	Absent	Absent	Present	Absent	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Present	Not seen	0
195	Absent	Absent	Present	Present	Infiltrating	No significant response	Absent	Shows lymphocytic embolisation by tumor cells	Absent	0	16	Not recovered	Not recovered	0	2	0	18	0	Absent	Not seen	7
196	Absent	Absent	Absent	Absent	Infiltrating	Mild	Absent	Free	Absent	Not recovered	Not recovered	0	8	Not recovered	Not recovered	0	8	0	Absent	Not seen	0
197	Absent	Absent	Present	Absent	Infiltrating	No significant response	Absent	Free	Absent	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Absent	Not seen	0
198	Present	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Absent	0	13	Not recovered	Not recovered	Not recovered	Not recovered	0	13	0	Absent	Not seen	8
199	Present	Absent	Present	Absent	Infiltrating	Mild	Absent	Free	Not seen	4	20	Not recovered	Not recovered	0	11	0	31	2	Absent	Not seen	0
200	Present	Absent	Absent	Present	Infiltrating	No significant response	Absent	Free	Absent	0	12	Not recovered	Not recovered	0	4	0	16	0	Absent	Not seen	8
201	Absent	Absent	Absent	Absent	Infiltrating	No significant response	Absent	Free	Not seen	0	14	Not recovered	Not recovered	Not recovered	Not recovered	0	14	0	Absent	Not seen	8
202	Absent	Absent	Absent	Absent	Infiltrating	Marked	Absent	Free	Not seen	0	20	Not recovered	Not recovered	Not recovered	Not recovered	0	20	0	Absent	Not seen	8
203	Absent	Absent	Absent	Absent	Pushing	No significant response	Absent	Free	Not seen	0	16	Not recovered	Not recovered	0	1	0	17	0	Absent	Not seen	8

S. No.	PR (out of 8)	HER 2/ neu	FISH analysis (in case of equivocal HER 2/ neu)	Ki-67 Percentage of Positive Nuclei	Additional marker E-cadherin	Additional marker EMA	Additional marker CK	Additional marker p63	Additional marker Mammaglobin	Additional marker p40	Additional marker Vimentin	Additional marker SMA	Additional marker 34BE12	Additional marker Synaptophysin	Additional marker Chromogranin A	Additional marker CK 5/6	Additional marker SOX-10	Additional marker GATA-3	Molecular Subtype
187	8	Equivocal	Negative	70	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
188	0	Negative	Not applicable	85	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Diffuse moderate positive	Triple Negative
189	8	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
190	8	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
191	8	Negative	Not applicable	20	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
192	8	Equivocal	Positive	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
193	0	Negative	Not applicable	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Triple Negative
194	0	Negative	Not applicable	60	Intact	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Focal weak positive	Triple Negative
195	7	Negative	Not applicable	20	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Luminal-B
196	0	Negative	Not applicable	90	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Diffuse strong positive	Absent	Diffuse moderate positive	Triple Negative
197	0	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Focal strong positive	Absent	Diffuse strong positive	Triple Negative
198	8	Equivocal	Negative	70	Lost in most of the tumor cells; retained in few tumor cells	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
199	0	Positive	Not applicable	65	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	HER 2/ neu enriched
200	7	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
201	0	Negative	Not applicable	25	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Negative	Negative	Absent	Absent	Absent	Luminal-B
202	0	Negative	Not applicable	80	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Luminal-B
203	8	Negative	Not applicable	10	NSE, Synaptophysin, Chromogranin: Positive	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Positive	Absent	Absent	Absent	Luminal-A

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Subject:: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Priyanka Seth**, a student of your college for **MD Pathology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Correlation of histomorphological features with molecular subtypes of carcinoma breast .

Supervisor	Co-Supervisor:-	Co-Supervisor:-
Dr. Aminder Singh	Dr. Harpreet Kaur	Dr. Kunal Jain
Assoc. Prof.	Prof. & Head	Asst. Prof.,
Dept. of Pathology	Dept. of Pathology	Dept. of Oncology

The student may submit the thesis in triplicate alongwith the plan in triplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

CORRELATION OF HISTOMORPHOLOGICAL FEATURES WITH MOLECULAR SUBTYPES OF CARCINOMA BREAST

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

PATHOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

August, 2022

Dr. Priyanka Seth

DEPARTMENT OF PATHOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	CORRELATION OF HISTOMORPHOLOGICAL FEATURES WITH MOLECULAR SUBTYPES OF CARCINOMA BREAST
For the degree of	MD (PATHOLOGY)
Name of the candidate	Dr.Priyanka Seth
Supervisor	Dr.Aminder Singh, Associate Professor, Department of Pathology, DMCH, Ludhiana
Co-supervisor(s)	Dr.Harpreet Kaur, Professor and Head, Department of Pathology, DMCH, Ludhiana Dr.Kunal Jain, Assistant Professor, Oncology, DMCH, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: All cases of breast carcinoma undergoing immunohistochemistry (IHC) for molecular sub typing will be analyzed.

Aims & Objectives: To correlate histomorphological features with molecular subtypes [Luminal A-like, Luminal B-like (HER2-negative), Luminal B-like (HER2-positive), HER2-positive (non luminal) and Triple-negative] of carcinoma breast.

Material & Methods: This will be a prospective study conducted in department of Pathology, DMCH, Ludhiana over the period of 1 year from September 15, 2022 to September 14, 2023. In this study, all histopathologically diagnosed breast carcinoma cases on trucut biopsies, mastectomy, breast conservation surgery (BCS) and lumpectomy specimens requiring IHC Studies will be included. Molecular subtypes will be determined using expression of ER, PR, HER-2/Neu and Ki 67. Additional IHC markers will be put, wherever required. Correlation of molecular subtypes with histomorphological features and grade will be done.

Clinical Significance: To obtain a good database for accuracy of the diagnosis of immunohistochemistry and its correlation with the histomorphological findings of carcinoma breast.

Keywords: Breast, Carcinoma, Histomorphological, Immunohistochemistry (IHC)

(Signature) Candidate	(Signature) Co-supervisor	(Signature) Co-supervisor	(Signature) Supervisor	(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"CORRELATION OF HISTOMORPHOLOGICAL FEATURES WITH MOLECULAR SUBTYPES OF CARCINOMA BREAST"** exist in the Department of Pathology, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

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APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
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Topic of Thesis	CORRELATION OF HISTOMORPHOLOGICAL FEATURES WITH MOLECULAR SUBTYPES OF CARCINOMA BREAST
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Date of enrollment	7th March, 2022
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Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
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PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

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4	DATE OF ADMISSION OF COURSE	07-03-2022
5	TITLE OF THE TOPIC	CORRELATION OF HISTOMORPHOLOGICAL FEATURES WITH MOLECULAR SUBTYPES OF CARCINOMA BREAST

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Breast Carcinoma is the most common malignancy among both-developed & developing countries. It is ranked as the 5th most common cause of death amongst cancers overall[1]. It constitutes 23% of all cancer patients and accounts for 14% of cancer related deaths[2]. In 2018, a total of 2.1 million women were diagnosed with breast cancer, which approximately accounts for one new case diagnosed every 18 seconds[3].

In the United States, approximately 230,000 new cases are diagnosed annually and approximately 40,000 patients die from the disease each year. The incidence is high in North America and northern Europe (92 new cases per 100,000 women/year), intermediate in southern European and Latin American countries, and low in most Asian and African countries[4].

In Brazil, according to the latest publication for the 2020-2021 biennium, produced by the National Cancer Institute (INCA), approximately 66, 280 new cases of breast cancer occur annually, with an estimated risk of 61.61 cases per 100 thousand women[3].

Incidence of breast carcinomas in India is lower as compared to the west. In India, it is the 2nd leading cause of cancer among women preceded by cervical carcinoma[1]. A woman who lives to age 90 has a one in eight chance of developing breast cancer. It is both ironic and tragic that a neoplasm arising in an exposed organ, readily accessible to self-examination and clinical diagnosis, continues to exact such a heavy toll[5]. However, male breast cancer is a relatively uncommon disease accounting for <1% of breast cancer incidence[6].

Traditionally, breast cancer has been classified by tumor stage. Morphological features, namely histological tumour type, tumour grade, proliferation status and lymphovascular invasion, have also been recognized as important prognostic variables.

The breast cancer is caused by a heterogeneous group of tumours, and the tumour behaviour and response to therapy is determined by its

underlying biological features. The widespread use of radiological screening, the greater availability of systemic therapy options and the move towards precision medicine drove the transition from purely prognostic classification systems to those which predict the response to various therapeutic modalities. The current morphological surrogates based on the anatomical and histological properties of the tumour neither reflect the biological and molecular heterogeneity of breast cancer, nor do they fully explain the genetic abnormalities found in tumours. While, the molecular biomarkers can predict the behavior and response to therapy[7].

Hence, the need to conduct this study is to correlate the histomorphological features of breast carcinoma with its molecular subtypes as these molecular subtypes are recognized to be associated with the outcome of therapy. They provide a framework for understanding the mechanism of breast carcinogenesis, and opportunities for improving the therapeutic intervention[8]. The management of patients with breast cancer remains critically dependent on careful pathological evaluation supplemented by ER, PR, HER-2/neu and Ki-67 test results[9].

6.2 REVIEW OF LITERATURE

The breasts (mammary glands) are highly modified apocrine sweat glands which develop embryologically along two lines, the milk lines, extending from the axillae to the groin. In humans, only one gland develops on each side of the thorax, although accessory breast tissue may be found anywhere along the milk lines. The breasts of both sexes follow a similar course of development until puberty, after which the female breasts develop under the influence of pituitary, ovarian and other hormones.

Until the menopause, the breast undergo cyclical changes in activity which are controlled by the hormone of the ovarian cycle. After menopause, like the other female reproductive tissues, the breasts also undergo progressive atrophy and evolutional change[10].

Risk factors for carcinoma breast:

The incidence rises throughout a women's lifetime, peaking at the age of 75-80 years and then declining slightly thereafter. Age of menarche, age at first live birth, reproductive history (number and timing of pregnancies), breastfeeding, diet, obesity and physical activity all probably play a role. The risk of breast cancer increases with number of affected first degree relatives (mother, sister or daughter), especially if the cancer occurred at a young age. A history of prior breast biopsies, especially if revealing atypical hyperplasia, increases the risk of invasive carcinoma. Non- Hispanic white women have the highest rate of breast cancer. Exogenous estrogen exposure, contraceptive agents, high breast density, ionizing radiation exposure and carinoma of contralateral breast or endometrium are strong risk factors for developing the cancer. The risk is higher for women with germline mutations in high risk breast cancer genes such as BRCA1 and BRCA2. Environmental contaminants such as organochlorine pesticides have estrogenic effects on humans[5].

Thus, all the factors listed above, act as major risk factors for the development of breast cancer in general poulation.

Invasive breast cancers (IBCs) are heterogenous, showing distinct molecular, pathologic features and biological behavior[8].

Invasive breast carcinoma almost always presents as a palpable mass. Palpable tumors are associated with axillary lymph node metastases in over 50% of patients. Larger carcinomas may be fixed to the chest wall or cause dimpling of the skin. When the tumor involves the central portion of the breast, retraction of the nipple may develop. Lymphatics may become involved so as to block the local area of skin drainage and cause lymphedema and thickening of the skin. In such cases, tethering of the skin to the breast by Cooper ligaments is referred to as peau d' orange[5].

Morphology of invasive carcinoma, No Special Type (NST; Invasive Ductal Carcinoma): On gross examination, most tumors are firm to hard and have an irregular border. When cut or scraped, they typically produce a characteristic grating sound due to small, central pinpoint foci or streaks of chalky-white elastotic stroma and occasional small foci of calcification. Less frequently, carcinomas have well-circumscribed border and a softer consistency[5].

WHO classification of epithelial tumours of breast (5th Edition, 2019):

Invasive breast carcinoma

Infiltrating duct carcinoma not otherwise specified (NOS)
Oncocytic carcinoma
Lipid-rich carcinoma
Glycogen-rich carcinoma
Sebaceous carcinoma
Lobular carcinoma NOS
Tubular carcinoma
Cribriform carcinoma NOS
Mucinous adenocarcinoma
Mucinous cystadenocarcinoma NOS

Invasive micropapillary carcinoma of breast
Apocrine adenocarcinoma
Metaplastic carcinoma NOS[11]

Histological grade is assessed according to the Nottingham modification of **Bloom-Richardson system**. The criteria for inclusion of patients into this analysis is as follows: (a) patients with invasive breast carcinoma, (b) patients with available histological grade and lymph node status, and (c) available formalin-fixed, paraffin embedded samples with good quality[12].

Microscopic Grading in Breast Carcinoma
(Nottingham Modification of the Bloom-Richardson system)

The Nottingham Grading System (NGS) when adequately carried out, provides a simple, inexpensive, accurate, and validated method for assessing patient prognosis. The NGS is based on the evaluation of three morphological features: (a) degree of tubule or gland formation, (b) nuclear pleomorphism, and (c) mitotic count[13].

Tubule formation

1 point: Tubule formation constitutes more than 75% of the tumor,
2 points: Tubule formation constitutes 10-75% of the tumor,
3 points: Tubule formation constitutes less than 10% of the tumor.
Note: Tubule formation evaluation should take into account the entire tumor.

Nuclear pleomorphism

1 point: Nucleus shape and size difference mild (Mild Nuclear Pleomorphism),
2 points: Nucleus shape and size difference moderate(Moderate Nuclear Pleomorphism),
3 points: Nucleus shape and size difference significant (Marked Nuclear Pleomorphism).
Note: The area containing cells with most prominent nuclear pleomorphism should be evaluated.

Mitotic Count

Mitotic counting process should only be done at the periphery of the tumor and should be started from the most mitotic active areas. The suggested application is counting within the same field. Areas rich in tumor that are free of normal breast tissue are preferred as much as possible. Prophase cells should not be counted. Due to differences in image area due to varying brands of microscopes, there are determined and accepted values for the number of mitotic count. Based on these values mitotic count are scored as 1, 2 and 3[2].

Score thresholds for mitotic counts based on the diameter of the high-power field and its corresponding area[11]:

Field diameter (mm)	Field area (mm2)	Mitotic count		
		1	2	3
0.40	0.126	≤4	5-9	≥10
0.41	0.132	≤4	5-9	≥10
0.42	0.138	≤5	6-10	≥11
0.43	0.145	≤5	6-10	≥11
0.44	0.152	≤5	6-11	≥12
0.45	0.159	≤5	6-11	≥12

A total score is obtained by scores on tubule formation, nuclear pleomorphism and mitotic count. The histological grade is determined based on the obtained total score[2].

Histologic type scoring:

Total score	Histologic Grade
3-5	I
6-7	II
8-9	III

Estrogen Receptor (ER)

ER is a nuclear protein with 1 DNA-binding domain and 2 activation function domains. A total of 65% to 75% of IBCs express ER, with ER being a major contributor to its development. Clinically, ER-expressing IBCs are usually better differentiated, have a favorable prognosis, and respond to hormonal therapy[8].

Progesterone Receptor (PR)

PR is also a transcription factor (similar to ER), largely controlled by ER and to some degree by growth factors as well, and is expressed in 55% to 65% of IBCs. In most cases, PR co-expresses with ER. Clinically, loss of PR suggests a more aggressive behavior and less response to hormonal therapy[8].

Human epidermal growth factor Receptor– 2 (HER-2)

HER2 encodes a transmembrane tyrosine kinase receptor that binds to its extracellular signals and initiates a signaling cascade mediating cell proliferation and survival. About 12% to 20% of IBCs either over-express the HER2 protein and/or have HER2 gene amplification, resulting in aggressive tumor growth and poor clinical outcome[8].

Ki-67

Ki-67 is a nuclear marker for proliferation expressed in all phases of the cell cycle except G0. Clinically, higher Ki-67 expression is usually associated with a higher grade and more aggressive behavior of the tumor. Nuclear staining of any intensity is evaluated. Currently, there is no standardized cut off value for Ki-67[8]. However, a threshold of 14% has been proposed for helping discriminate between more aggressive Luminal B molecular subtype and less aggressive Luminal A subtype. Molecular subtype Luminal B has Ki-67 proliferation index of more than/equal to 14% whereas Luminal A has Ki-67 proliferation index of less than 14% [11].

Morphologically, there are 21 distinct subtypes of IBCs as defined by the World Health Organisation (WHO) classification (5th edition, 2019). Currently, the morphological classification, histological grade, status of

ER, PR, HER-2, Ki-67, alongwith tumor stage , are used to guide the clinical management of carcinoma breast[8].

Breast cancer is classified into molecular subtypes based on the expression of above mentioned four markers. The various molecular subtypes are as follows:

- Luminal A-like
- Luminal B-like (HER2- negative)
- Luminal B-like (HER2- positive)
- Her-2/neu positive (non-luminal)
- Triple-negative type[11]

Luminal A-like is defined as ER and PR-positive, HER2-negative Ki-67 low (less than/ equal to 10%)[7]. It has a small tumor size, the best prognosis and the lowest recurrence rate than other subtypes[14].

Luminal B-like is subclassifed into Luminal B HER2- positive and Luminal B HER2- negative but with either high proliferative activity (Ki-67 more than/ equal to 30%) and PR low[7]. It has an aggressive phenotype and worse prognosis compared to Luminal A[14].

HER 2/ neu positive is defined as HER-2 overexpression/ gene amplification with absence of ER and PR[7]. This subtype has a poor prognosis, and characterized by high proliferation rates[14]. Due to its predictive value, HER-2 is currently the most important theranostic test for breast cancer. Accurate assessment of HER-2 status is critical, and the lesson learned from HER-2 testing will be applied for future biomarkers assessment. Scoring criteria should be rigidly followed so that there are no 3+ false positive(s) or 1+ false positive(s). All 2+ cases should go for reflux Fluorescence In Situ Hybridization (FISH) testing[15].

The **Triple negative** is defined as the negative expression of ER, PR and lack of over-expression and amplification of HER2 gene. It accounts for about 10-20% of all breast cancers and also accounts for most of the deaths due to breast cancer[16]. This subtype has been recognized to show the most aggressive behavior with the worst outcome[14].

The cancers will be staged according to the **TNM** system.

T – Denotes size of the tumor

N – Denotes the spread of the tumor to nearby lymph nodes

M – Denotes that cancer has undergone metastasis i.e. it has spread and infected other part(s) of the body[17].

A number of studies have been done in literature correlating the morphological features and various types of carcinoma breast with ER, PR, HER-2/neu and Ki-67 labelling index.

In a study conducted by **R kornegoor et al.** in 2011 in Netherlands on 'molecular subtyping of male breast cancer by immunohistochemistry', 134 cases of male breast cancer were immunohistochemically stained for ER, PR, HER2, Ki-67, epidermal growth factor receptor (EGFR), Cytokeratin 5/6 (CK5/6) and CK14. Cases were classified as Luminal A, Luminal B, HER2 driven, basal-like, or unclassifiable triple negative. Out of all, Luminal A (representing 75% of cases) was the most encountered type of male breast cancers followed by Luminal B (21%), followed by the basal-like and unclassifiable triple negative (4%). HER2 driven cases were not identified[6].

Tiwari et al. in Madhya Pradesh, conducted a cross sectional study on 70 IBC samples from November 2012 to October 2014 and correlated the molecular classification with their clincohistopathology. The cases were subclassified using ER, PR, HER-2/neu, Ki-67, CK 5/6 into Luminal A, Luminal B, HER-2/neu positive, basal-like and normal-like subtypes. The most common molecular subtype was found to be Luminal A (representing 27.1% of total cases), while the least common subtype was found to be normal-like (representing 5.7% of total cases). Thus, they concluded that histological classification alone was not able to evaluate the biological behavior of the different breast tumors; and molecular classification was useful and superior to the histological classification, both for clinical management and for short time prognostic value[1].

A study was done by **Karangadan et al.** in 2016 at Lady Hardinge Medical college, New Delhi. Breast carcinoma was classified into four molecular subtypes - Luminal A, Luminal B, triple negative and HER2 positive based on the IHC patterns. 60 cases of breast carcinoma were studied over a period of 3 years. Correlation of the four subtypes with Ki-67 was done. Out of these 60 cases, the most common molecular subtype was found to be triple-negative (40.00%) followed by luminal B (23.33%). Most of the tumors showed low proliferative index; however, triple negative and HER2 positive subtype showed high proliferative index. Thus, they concluded that correlation of molecular classification with histological grade and Ki-67 was statistically significant ($p < 0.05$); and molecular subtypes correlated with the prognosis and aided in the targeted therapy[18].

A retrospective study on intrinsic molecular subtypes of breast cancer in patients in Indonesia was conducted by **Swandari Paramita et al.** in 2019. 92 invasive ductal breast carcinoma patients were included in the study. Immunohistochemical staining using anti-ER, PR, HER-2 and ki-67 antibodies was applied to classify intrinsic molecular subtypes. An association between clinical and immunohistochemical factors with intrinsic molecular subtypes of breast cancer were analyzed. Luminal B (42.39%) was found to be the most common intrinsic molecular subtype of breast cancer, followed by HER-2 positive (39.13%), triple-negative (10.87%), and luminal A (7.61%). The study also revealed a significant association between patient's age with molecular subtypes of breast carcinoma. Luminal B was the most common subtype in patients aged less than / equal to 35 years, while HER-2 positive was the most common subtype in older patients. Thus, age was also found to be associated with intrinsic molecular subtypes of breast carcinoma[14].

A cross sectional study on ‘histomorphological correlation of breast carcinoma with its molecular classification’ in Rajasthan was conducted by **Soni et al.** in 2020. 500 cases of breast carcinoma were included. They correlated molecular subtypes with histological grade and

prognostic factors. Out of these 500 cases, maximum number of cases were found to be Luminal A (38.20%) (molecularly); and infiltrating duct carcinoma NOS followed by lobular carcinomas (histologically)[19].

A population-based case-control study of genes implicated in breast cancer was done by **Chunling Hu et al.** in 2021 in the U.S. population. The purpose of their study was to identify germline pathogenic variants in 28 cancer-predisposition genes among 32,247 women with breast cancer (case patients) and 32,544 unaffected women (controls). Among the case patients, the highest prevalence of pathogenic variants was observed for BRCA (1.29%; 95% CI), CHEK (1.08%; 95% CI), and BRCA1 (0.85%; 95% CI). They found the mean age of breast cancer diagnosis among the case patients to be 62.1 years, and 61.2 years among the controls. A family history of breast cancer was reported in 20.4% of case patients and 14.3% of controls. Among the case patients, 82.9% had ER-positive breast cancer and 11.3% had triple-negative breast cancer. Thus, risk assessment and breast cancer management in women with inherited pathogenic variants was the basis of their study[20].

6.3 AIMS AND OBJECTIVES OF THE STUDY

To correlate histomorphological features with molecular subtypes [Luminal A-like, Luminal B-like (HER2-negative), Luminal B-like (HER2-positive), HER2-positive (non luminal) and Triple-negative] of carcinoma breast.

7. MATERIAL AND METHODS

All the trucut biopsies, mastectomy, breast conservation surgery (BCS) and lumpectomy specimens that will be received in the department of Pathology, DMCH, Ludhiana and diagnosed as breast carcinoma cases on histopathology, on which IHC will be done will be included in the study. A detailed history including age, sex, parity, family history, menstrual history, lactational history, mammography and metastatic workup (wherever available) will be obtained[19].

7.1 Source of data

This will be a prospective study to be conducted in department of Pathology, DMCH, Ludhiana over the period of 1 year from September 15, 2022 to September 14, 2023. In this study, all histopathologically diagnosed breast carcinoma cases requiring IHC studies will be included. Molecular subtypes will be determined using expression of ER, PR, HER-2/Neu and Ki 67. Additional IHC markers will be put, wherever required. Correlation of molecular subtypes with histological grade, prognostic and predictive features will be done[19].

7.2 METHOD AND COLLECTION OF DATA

INCLUSION CRITERIA

All cases of breast carcinoma undergoing IHC for molecular sub typing.

EXCLUSION CRITERIA

- All non-neoplastic lesions and non-epithelial tumours of breast.
- All cases of carcinoma breast in which IHC is not done.

Methodology:

In this study, trucut biopsy, mastectomy and breast conservation surgery (BCS)/ lumpectomy specimens received will be properly sliced & fixed in 10% formalin for 18-20 hrs. Detailed gross examination will be done. The tissue sections will be stained with H&E and detailed HPE will be done as per College of American Pathologists (CAP) Protocol. Sections from tumor will be subjected for IHC staining[19].

For IHC, staining of slides prepared from formalin fixed paraffin embedded tissue (FFPET) on the BenchMark Classic Automated System (from Ventana) will be done. Sections from FFPET biopsies will be cut using the microtome at 3-4 micron thickness and will be mounted onto SuperFrost Plus slides. For each slide, Ventana labels will then be printed which will include a unique barcode containing all protocol information. The slides will then be loaded onto the BenchMark carousel and read by the Ventana Barcode Reader. The automated BenchMark system will put the slides through a series of user-defined de-paraffinization and antigen retrieval steps before commencing with the antibody staining. Primary antibody will either be applied automatically if in a pre-diluted dispenser or otherwise will manually be titrated onto the slide. The pre-diluted dispensers of the Ultraview Universal DAB detection kit will then provide all reagents required for staining. The counterstain and post-counterstain comprise haematoxylin and bluing reagent. Hence, each case will be stained for ER, PR, Her-2/neu, Ki 67 and then subclassified into luminal A-like , luminal B-like (HER2-negative), Luminal B-like (HER2-positive), HER2-positive (non-luminal) and Triple-negative subtypes.

HER-2/neu 2+ cases will be subjected to Fluorescence in situ hybridization (FISH) and the final molecular categorization will be done accordingly.

Interpretation of IHC study:

- ER/PR reporting - Nuclear positivity is assessed in tumor cells and percentage of tumour cells showing positivity, staining intensity (graded as 1+ = weak staining , 2+ =moderate staining and 3+ as strong staining are noted) [19].

Allred scoring system can be used to combine the intensity and percentage information for an overall score.

Allred scoring system[15]:

Proportional Score (PS)
0: No staining
1: Staining of less than 1% of tumor cells

2: Staining between 1% and 10% of tumor cells
3: Staining between 1/10 and 1/3 of tumor cells
4: Staining between 1/3 and 2/3 of tumor cells
5: Staining of more than 2/3 of tumor cells

Intensity Score (IS)
0: No staining
1: Average weak intensity
2: Average moderate intensity
3: Average strong intensity

Allred score (range, 0 to 8) = PS+IS[15]. The Allred scoring system has an 8-point scale (0–8). This scoring system is calculated by adding the number representing the proportion of positive cells 0, 1, 2, 3, 4, or 5 to the number reflecting the intensity of the nuclear stain 0, 1, 2, or 3 . Tumors with a score of less than 3 show usually a poor response to the anti-estrogen therapy[21].

- HER2/neu reporting -The literature regarding HER2 IHC testing suggests that 2+ score is the most problematic, however, we believe that it is the 1+ or 3+ scores which are often misinterpreted. We would do FISH for HER2 gene copy number assessment when the IHC score is 2[15] .

IHC interpretation:

Positive: 3+: Circumferential membrane staining that is complete, intense and in >10% of tumour cells.

Equivocal: 2+: Weak to moderate complete membrane staining observed in >10% of tumour cells.

Negative:

- 1+: Incomplete membrane staining that is faint / barely perceptible and in > 10% of tumour cells

- 0: No staining is observed, or incomplete membrane staining that is faint / barely perceptible and in less than/ equal to 10% of tumour cells[11]

- Ki-67 labeling index - Percentage of positive nuclei are expressed as a "Ki-67 labeling index" which is the percentage of cells expressing Ki-67 determined by counting 1000 cells / slide[19]. ER-positive cancers have a wider range of proliferation, with highly proliferative forms correlated with more-aggressive behaviour, although most cases have a Ki-67 proliferation index < 20%. A threshold of 14% has been proposed for helping to discriminate between cases likely to correlate with the more aggressive luminal B molecular subtype (have Ki-67 proliferation index more than/ equal to 14%) versus the less aggressive luminal A subtype (have Ki-67 proliferation index < 14%). However, this threshold has not been validated for predicting the response to chemotherapy[11].

DURATION OF STUDY

This will be a 1 year prospective study from September 15, 2022 to September 14, 2023.

OUTCOME

Histomorphological and IHC findings of breast carcinomas will be documented according to the protocol.

STATISTICAL ANALYSIS

Data will be described in terms of range; mean +/- standard deviation (+/-SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using SPSS (Statistical Package for The Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith.

.

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PROFORMA

Sr. No. _____

Patient's name : Age/ Sex:

Address: MRD no. :

Histopathology No.: IHC No. :

Date of receiving the sample:

Date of reporting :

Clinical history/ History of presenting illness :

- Breast lump : Present/ Absent
- Duration of breast lump (if present):
- Swelling in axilla : Present/ Absent
- Symptoms suggestive of metastasis : Present/ Absent

Personal history :

- Menstrual history :
- Parity :
- Last child birth :
- Lactational history/ Breastfeeding : Present/ Absent
- Intake of Oral Contraceptive Pills (OCPs) : Present/ Absent

Past history:

- History of ovarian or any other carcinoma : Present/ Absent
- History of known gene mutations (BRCA1/BRCA2) : Present/ Absent

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Family history :

- History of carcinoma breast in the first-degree relatives/ family members : Present/ Absent
- History of ovarian or any other carcinoma in the first-degree relatives/ family members : Present/ Absent

Clinical Diagnosis:

- Clinical stage : ____ cT ____ cN ____ cM (Stage: _____)

- Laterality : Left/ Right/ Bilateral/ Not specified

- Quadrant : Upper outer quadrant/ Lower outer quadrant/ Upper inner quadrant/ Lower inner quadrant/ Central/ Nipple

Response to chemotherapy : Present/ Absent

(in case of post-therapy cases)

Imaging Studies:

- Mammography :

- USG Breast :

- Chest Xray

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- MRI:

- CT scan:

- PET scan:

Gross examination:

- Procedure: Excision (less than total mastectomy)/ Total mastectomy (including nipple-sparing and skin-sparing mastectomy)/ Trucut/ Breast Conservation Surgery (BCS)/ Total Mastectomy +/- Axillary Dissection/ Other group of lymph nodes/ Not specified
- Other (specify): _____
- Measurement of specimen: ____X____X____ cms
- Status of overlying skin: Ulcerated/ Previous surgery scar/ Nodules
- Nipple retracted: Yes/ No
- Growth: Present/ Absent
- Number of lesions: Solitary/ Multiple
- Size of growth: _____X_____X____ cms
- Growth Site: Upper outer quadrant/ Lower outer quadrant/ Upper inner quadrant/ Lower inner quadrant/ Central/ Nipple
- Clock position: _____ o' clock
- Distance from nipple : _____ cm/ Not specified
- Other (specify): _____
- Consistency of growth: Hard/ Firm/ Rubbery/ Soft

- Distance from deep resected margin: ____cms and ____cms from overlying skin
- Skeletal muscle: Present/ Absent
- Number of (A) Regional lymph nodes: _____recovered with size_____ cms, Consistency: Hard/ Firm/ Rubbery/ Soft
- Number of (B) Sentinel lymph nodes: _____recovered with size_____ cms, Consistency: Hard/ Firm/ Rubbery/ Soft
- Number of (C) Level 3 lymph nodes: _____recovered with size_____ cms, Consistency: Hard/ Firm/ Rubbery/ Soft
    - Size of the largest lymph node involved: _____ cm
    - Size of the largest deposit: _____ cms/ Cannot be determined

Histopathological Examination:

- Histopathological type: _____
- Modified Bloom Richardson score and grade:
    - Total score Histologic Grade

        3-5 I

        6-7 II

        8-9 III

Interpretation of Modified Bloom Richardson score: A total score is obtained by adding scores of tubule formation, nuclear pleomorphism and mitotic count.

(A) Glandular (Acinar) / Tubular Differentiation:

Score 1: Tubule formation constitutes more than 75% of the tumor,

Score 2: Tubule formation constitutes 10-75% of the tumor,

Score 3: Tubule formation constitutes less than 10% of the tumor.

(B) Nuclear Pleomorphism:

Score 1: Nucleus shape and size difference mild (Mild Nuclear Pleomorphism),

Score 2: Nucleus shape and size difference moderate (Moderate Nuclear Pleomorphism),

Score 3: Nucleus shape and size difference significant (Marked Nuclear Pleomorphism).

(C) Mitotic Rate:

Score 1: ≤5 mitosis/ 10 hpf

Score 2: 6-10 mitosis/ 10 hpf

Score 3: ≥11 mitosis/ 10 hpf

- Margins: Infiltrating/ Pushing
- Lymphocytic response at the advancing margins: Mild/ Moderate/ Marked
- Lymphovascular embolization: Present/ Absent
- Perineural invasion: Present/ Absent
- Necrosis: Present/ Absent
- Sclerosis: Present/ Absent
- Microcalcifications: Present/ Absent
  - Microcalcifications present in: DCIS/ invasive carcinoma/ non-neoplastic tissue
- Deep resected margin: Involved/ Free
- Skeletal muscle involvement: Present/ Absent
- Skin invasion: Present/ Absent

- Nipple invasion: Present/ Absent
- Paget's disease: Present/ Absent
- Intraductal component: Present/ Absent
  - Pattern of DCIS (Type):
  - Grade of DCIS:
  - Percentage of tumor area: _____%
- Lymph nodes:

(A) Regional lymph nodes: Present/ Absent

Number positive for metastasis out of total regional LN's:

(B) Sentinel lymph nodes: Present/ Absent

Number positive for metastasis out of total sentinel LN's:

(C) Level 3 lymph nodes: Present/ Absent

Number positive for metastasis out of total level 3 LN's:

Total number of lymph nodes involved out of all LN's:

- Size of largest involved lymph node:
- Extranodal Extension: Present/ Absent

- Treatment induced changes in breast: Present/ Absent
- Treatment induced changes in lymph node: Present/ Absent
- Margin status: Involved/ Not involved
  - Distance from carcinoma to margins: _____ mm
- Distant metastais: Not applicable/ Non-regional lymph nodes(s)/ Lung/ Liver/ Bone/ Brain/ Other/ Cannot be determined

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Pathological TNM Stage: _____

IHC Findings:

- ER= Proprtional Score + Intensity Score= _____
- PR= Proprtional Score + Intensity Score= _____
- HER2 neu= _____
- Ki-67 Percentage of Positive Nuclei=_____ %
- Any additional IHC marker and it's interpretation: _____
- Comment(s): _____

Interpretation of IHC markers:

- ER/ PR scoring system and criteria as per Allred scoring system:

Proportion Score:

0= No cells are ER positive.

1= ≤1% of cells are ER positive

2= 1-10% of cells are ER positive

3= 11-33% of cells are ER positive

4= 34-66% of cells are ER positive

5= 67-100% of cells are ER positive

Intensity Score:

0= Negative

1= Weak

2= Intermediate

3= Strong

Total (PS+IS) 0-2= Negative, 3-8= Positive

- HER2 neu:

Negative: 0: No staining is observed, or incomplete membrane staining that is faint / barely perceptible and in less than/ equal to 10% of tumour cells.

1+: Incomplete membrane staining that is faint / barely perceptible and in > 10% of tumour cells

Equivocal: 2+: Weak to moderate complete membrane staining observed in >10% of tumour cells.

Positive: 3+: Circumferential membrane staining that is complete, intense and in >10% of tumour cells.

- FISH report: _____

(In case of HER-2/neu 2+ positive tumors)

- **Molecular Subtype:** _____

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